Prosodic and Semantic Affect Perception in Remitted Patients With Bipolar I Disorder

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ABSTRACT

Objective: Bipolar disorder is associated with impairments in emotion processing that are present during both mood episodes and periods of remission. In this context, most previous studies have investigated facial emotion recognition abilities. In contrast, the current study focused on the perception of prosodic and semantic affect.

Method: The present study directly contrasted the perception of prosodic and semantic affect in 58 remitted patients meeting *DSM-IV* criteria for bipolar I disorder and 45 healthy volunteers by using 2 subtests of the Comprehensive Affective Testing System (CATS) and investigated the relationship of prosodic and semantic affect perception with patients' outcomes. Participants were investigated from June 2011 until May 2013.

Results: Patients and controls did not differ regarding the recognition of the vocal emotion while ignoring the affective meaning of test trials (CATS 1), but patients significantly more often misinterpreted sad as happy prosody ($P = .039$). In addition, patients were impaired in recognizing the affective meaning of test trials while ignoring the vocal emotion (CATS 2; $P = .052$). Again, they significantly more often misinterpreted a sad affective meaning as a happy one ($P = .025$). However, the findings on misinterpretations did not withstand Bonferroni correction for multiple testing. CATS 1 test performance was negatively correlated with depression scores, whereas a positive association was found between performance on both tests and patients' functioning. Patients indicated a significantly lower quality of life ($P < .001$); however, multiple mediation analysis revealed that this finding was not mediated by differences in prosodic and/or semantic affect perception between the 2 groups.

Conclusions: Even during periods of remission, patients with bipolar disorder may be impaired in semantic but not prosodic affect perception. Notably, they may frequently misinterpret sadly expressed emotions as happy ones. Our findings underscore the relevance of these deficits in the psychosocial context.

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Several studies report on impairments in emotion processing in patients with bipolar disorder. These deficits are present during both mood episodes and periods of remission and have been demonstrated to have a negative impact on patients' outcome.[1–3]

So far, the bulk of research has investigated facial emotion recognition abilities. However, in addition to this visual way of expressing emotions, auditory signals represent another modality to communicate emotions. Accordingly, the ability to accurately perceive, interpret, and process emotion from prosodic intonation (affective prosody) and to understand the affect inherent in the meaning of sentences are important aspects of human social communication.

While a number of studies have focused on affective prosody perception in patients suffering from major depressive disorder,[4–7] only a few investigations have dealt with affective prosody perception in patients with bipolar disorder, and they have provided divergent findings.[8–11] Vaskinn et al,[8] for example, detected no deficits, but Bozikas et al[9] reported on impairments in female patients with bipolar disorder who performed more poorly in the recognition of fear and surprise than healthy women, whereas male patients did not differ from their healthy consexuals in this regard.

We recently studied the impact of facial emotion recognition abilities on subjective and functional outcomes in patients with bipolar disorder who were in remission.[12] Patients were particularly impaired in the recognition of disgust and happiness, and the correct identification of happy faces was significantly associated with lower depression scores and higher quality of life (QoL) scores. In contrast, Fulford et al[13] found the correct identification of fearful faces to predict patients' QoL. Importantly, the impact of prosodic and semantic affect perception on patients' QoL had yet to be investigated.

Investigating an extended sample, we have now examined prosodic and semantic affect perception in remitted patients with bipolar disorder compared to healthy control subjects. In light of the inconsistent findings of previous studies,[9,11,14] we were also interested in potential gender-specific differences. In addition, we investigated the relationship between prosodic and semantic affect perception and patient outcomes in terms of psychopathology and psychosocial functioning. Moreover, we studied whether prosodic/semantic affect perception might act as a mediator between diagnosis (BD patients vs controls) and QoL.

METHOD

This study included 58 remitted outpatients meeting *DSM-IV* diagnostic criteria for bipolar I disorder and 45 healthy controls between 18 and 60 years of age. Participants were investigated from June 2011 until May 2013. Patients were recruited from the outpatient

Clinical Points

- Even during periods of remission, patients with bipolar disorder may be impaired in semantic but not prosodic affect perception, which interferes with functioning.
- Next to psychopharmacologic treatments, psychosocial interventions are needed to improve affect recognition, social cognition, and functioning.

units of the Medical Universities Innsbruck and Salzburg in Austria. Healthy controls from the community were chosen to match patients in age, sex, and education. Control subjects were free of medication that might impede task performance. The study received approval by the ethics committees of both universities. All participants gave written informed consent.

In patients, the diagnosis of bipolar disorder was confirmed by using the Mini-International Neuropsychiatric Interview (MINI).[15] To ensure symptomatic remission, scores of ≤ 8 on both the Young Mania Rating Scale (YMRS)[16] and the Montgomery-Asberg Depression Rating Scale (MADRS)[17] were required. Prerequisites for healthy participants included a score of ≤ 63 on the Brief Symptom Inventory (BSI)[18] and a negative history of any psychiatric illness. Exclusion criteria for both groups included current or past neurologic, audiological, or developmental disorders, traumatic brain injury, a history of any other Axis I disorder, and physical illness that might interfere with the participants' cognitive performance. Premorbid intelligence was measured by using the German adaptation of the National Adult Reading Test,[19] the Mehrfachwahl-Wortschatz-Test-B (MWT-B).[20]

Prosodic and Semantic Affect Perception

Prosodic and semantic affect perception were assessed using 2 subtests of the Comprehensive Affective Testing System (CATS).[21] In subtest 9 (CATS 1), the subject was instructed to ignore the affective meaning represented in affect-laden sentences and focus on the prosody (happiness, sadness, or neutrality). In subtest 10 (CATS 2), the same sentences are presented as in CATS 1; however, subjects had to ignore the prosody and focus on the affect inherent in the meaning of the sentences, which can be happy, sad, or neutral. These tasks consist of 32 trials, of which 50% are congruent with regard to prosody and affective content. Participants were seated in a quiet room. Stimuli were offered via headphones.

Psychosocial Functioning

Next to the assessment of partnership/employment status and living situation, the overall level of patients' functioning was assessed using the Global Assessment of Functioning Scale (GAF).[22]

Quality of Life

Quality of life was assessed with the World Health Organization QoL, abbreviated version (WHOQOL-BREF),[23] which consists of 26 questions scored in 4 domains: physical health, psychological health, social relationships, and environment. Each question is rated on a 5-point Likert scale; domain scores are transformed to lie between 0 and 100.

Statistical Analysis

Depending on the variable type, the χ^2 test, the *t* test, and the Mann-Whitney *U* test were used for comparison of patients with bipolar disorder and healthy control subjects with respect to sociodemographic variables. The Mann-Whitney *U* test was also employed to compare the 2 groups with regard to prosodic and semantic affect perception and QoL, since a considerable part of the subscales showed a non-normal distribution. In addition, both prosodic affect perception and semantic affect perception were analyzed in 2 separate repeated-measures analyses of variance with affect (happy, sad, neutral) as a within-subjects factor and group (patients with bipolar disorder, controls) as a between-subjects factor. The effect of congruence versus incongruity of test trials on performance was investigated by means of the Wilcoxon matched-pairs test. Moreover, the effect of sex on prosodic and semantic affect perception, in addition to the group effect, was investigated by means of 2-way analysis of variance or ordinal regression, depending on the distribution of the dependent variable.

Within the patient group, associations between prosodic and semantic affect perception and both symptomatology and functioning were evaluated by means of nonparametric correlation analysis (Spearman rank correlation coefficient; point-biserial correlation coefficient for correlations of affect perception with dichotomous variables). The same method was also used to analyze associations between QoL and prosodic and semantic affect perception. In order to limit the number of statistical tests performed, only the CATS total scores were set into relation with the QoL subscales.

All statistical tests were performed at a .05 significance level. Both uncorrected and Bonferroni corrected *P* values were calculated.

In order to investigate the roles of prosodic and semantic affect perception as potential mediators between group and QoL, we performed a multiple mediation analysis with bootstrapped estimation of path coefficients (5,000 resamples) using the SPSS macro INDIRECT.[24] In this analysis, the diagnostic group served as the independent variable, global QoL as the dependent variable, and both prosodic and semantic affect perception as potential mediators. Due to the non-normal distribution, global QoL was subjected to a rank transformation prior to the analysis. For completeness, the same type of mediation analysis was also performed for the subscales of the WHOQOL-BREF.

Power Analysis

Under standard assumptions regarding type I and type II error ($\alpha = .05$, $\beta = .2$), the sample size of 58 patients with bipolar disorder and 45 controls is sufficiently large to detect, in a 2-tailed Mann-Whitney *U* test, group differences

Table 1. Sample Characteristics

Characteristics	Bipolar Patients	Controls
N	58	45
Age, mean ± SD, y	42.2 ± 11.8	39.6 ± 9.4
Female/male, %	34.5/65.5	28.9/71.1
Education, mean ± SD, y	13.0 ± 2.9	13.6 ± 1.9
Duration of illness, mean ± SD, y	13.5 ± 9.5	…
MADRS, mean ± SD	2.9 ± 2.3	…
YMRS, mean ± SD	1.1 ± 1.4	…
Premorbid intelligence (MWT-B), %	68.0 ± 25.6	70.6 ± 20.7
Treatment, n (%)		
Mood stabilizer monotherapy	9 (15.5)	…
Antipsychotic (AP) monotherapy	0 (0.0)	…
Antidepressant (AD) monotherapy	0 (0.0)	…
Mood stabilizer ± AP	20 (34.5)	…
Mood stabilizer ± AD	9 (15.5)	…
AP + AD	3 (5.2)	…
Mood stabilizer ± AP ± AD	16 (27.6)	…
Concomitant medication, n (%)		
Benzodiazepines	1 (1.7)	…
Housing, n (%)**		
With original family	6 (10.3)	0 (0.0)
With own family	27 (46.6)	34 (75.6)
Alone	23 (39.7)	10 (22.2)
In a small group home	0 (0.0)	0 (0.0)
Other	2 (3.4)	1 (2.2)
Partnership status, n (%)*		
Single	19 (32.8)	12 (26.7)
Married/stable partnership	15 (25.9)	29 (64.4)
Divorced/separated	12 (20.7)	4 (8.9)
Widowed	1 (1.7)	0 (0.0)
Employment status, n (%)**		
Full-time employment	13 (22.4)	29 (64.4)
Part-time employment	11 (19.0)	13 (28.9)
Supported employment	1 (1.7)	0 (0.0)
Training	3 (5.2)	2 (4.4)
Housewife	1 (1.7)	1 (2.2)
Retired	23 (39.7)	0 (0.0)
Unemployed	6 (10.3)	0 (0.0)

*$P = .028$ (χ^2 test).
**$P < .001$ (χ^2 test).
Abbreviations: MADRS = Montgomery-Asberg Depression Rating Scale, MWT-B = Mehrfachwahl-Wortschatz-Test-B, YMRS = Young Mania Rating Scale.

exceeding an effect size of $d = 0.575$. This is a medium effect size according to the classification given by Cohen.[25] Moreover, under the same conditions as above, the patient sample (n = 58) is sufficiently large to detect Spearman rank correlation coefficients exceeding a value of $P = .37$.

RESULTS

Sample Characteristics

Demographic and clinical characteristics are summarized in Table 1. Patients and control subjects were comparable with regard to age, sex, premorbid intelligence, and education. They differed significantly with regard to partnership/employment status and living situation.

Prosodic and Semantic Affect Perception

An overview of prosodic and semantic affect perception is given in Table 2. CATS 1 total scores were comparable in patients and controls. Only the recognition of neutral emotionality reached a trend level in favor of healthy subjects. Analysis by repeated-measures ANOVA yielded similar results. While there was a significant main effect of the factor affect ($F_{2,189} = 3.84$, $P = .026$; overall, happy and neutral prosody was recognized more easily than sad prosody, $P = .026$ and $P = .022$, respectively), no significant main effect of the factor group ($F_{1,101} = 1.49$, $P = .225$) and only trend-level significance for the group-by-affect interaction ($F_{2,189} = 2.57$, $P = .083$) were detected. Regarding misinterpretations, patients with bipolar disorder significantly more frequently misinterpreted sadly expressed emotions as happy ones, and, at a trend level, neutrally expressed emotions as sad ones. However, these findings did not withstand Bonferroni correction for multiple testing.

Compared to healthy control subjects, patients with bipolar disorder exhibited lower CATS 2 total scores at a trend level of significance. No significant group differences were seen for any of the CATS 2 subscales, although trend-level significance was attained for the recognition of sad emotions with poorer performance in patients with bipolar disorder. Again, analysis by repeated-measures ANOVA produced similar results. There was a highly significant main effect of the factor affect ($F_{2,148} = 175.9$, $P < .001$; overall, sadness was most easily recognized, followed by happiness and neutrality, always $P < .001$), whereas only trend-level significance was reached for the factor group ($F_{2,148} = 3.82$, $P = .053$). The group-by-affect interaction did not attain statistical significance. Regarding misinterpretations, patients significantly more often misinterpreted a sad affective meaning as a happy one; but again, significance was not retained after Bonferroni correction.

With 1 exception, men and women showed comparable performance in the CATS tests. A significant gender difference was detected regarding the recognition of neutral prosody (CATS 1) favoring male participants (90.5 ± 20.7 points in men vs 81.8 ± 23.9 points in women, $Z = 2.62$, $P = .009$). This applied for the sample as a whole (N = 103) and was likewise true for patients and controls, as there was no significant interaction between gender and group.

Both patients and controls performed significantly better on CATS 1 and CATS 2 trials that were congruent with regard to prosody and affective meaning as compared to those trials in which prosody and affective meaning differed from each other. On average, patients' CATS 1 scores were 23.2 ± 28.0 percentage points higher for congruent trials than for incongruent trials (controls: 17.1 ± 20.5 points; $Z > 4.5$, $P < .001$ in both cases). Similarly, patients scored 15.9 ± 29.0 points higher (controls 11.1 ± 19.1) in congruent trials of CATS 2 ($Z > 3.35$, $P < .001$) compared to incongruent trials,. However, there was no significant difference between patients and controls in this respect ($P > .1$), ie, both groups profited likewise from congruence of prosody and affective meaning.

Clinical Outcomes

Patients' mean GAF score was 82.0 ± 11.5 (range, 1–100), thereby reflecting a relatively high level of global functioning. Table 3 provides results concerning QoL. Patients achieved significantly lower scores than healthy control subjects in all life domains assessed.

Table 2. CATS 1 and 2: Total Scores and Subscores

	Group				Mann-Whitney U Test	
	Patients		Controls			
CATS 1	Mean	SD	Mean	SD	Z	*P* Value
Total score, %	80.15	20.04	84.71	12.30	−0.554	.586
Individual emotions, % correct						
Happy	83.33	20.71	84.81	17.25	0.010	.992
Sad	79.43	15.78	80.19	16.60	−0.354	.723
Neutral	80.60(↓)	25.99	89.72	17.93	−1.897	.058
Misinterpretations, %						
Happy as sad	6.47	11.15	3.33	6.74	0.934	.350
Happy as neutral	10.20	14.48	11.85	15.02	−0.519	.604
Sad as happy	2.59 ↑[a]	6.28	0.37	1.74	2.065	.039 ($P_{Bonferroni}$ = .234)
Sad as neutral	17.99	13.94	19.44	16.57	−0.179	.858
Neutral as happy	4.09	10.31	1.11	4.48	1.643	.100
Neutral as sad	15.30 (↑)	19.74	9.17	16.08	1.854	.064

	Group				Mann-Whitney U Test	
	Patients		Controls			
CATS 2	Mean	SD	Mean	SD	Z	*P* Value
Total score, %	65.95(↓)	8.58	68.96	5.81	−1.947	.052
Individual emotions, % correct						
Happy	71.41	15.22	72.78	13.69	−0.514	.607
Sad	80.46(↓)	16.11	86.48	10.85	−1.657	.098
Neutral	35.99	22.35	36.94	18.84	−0.494	.622
Misinterpretations, %						
Happy as sad	9.20	8.06	9.44	9.50	−0.095	.924
Happy as neutral	19.40	15.72	17.78	13.72	−0.368	.713
Sad as happy	3.74 ↑[a]	6.47	1.11	2.86	−2.246	.025 ($P_{Bonferroni}$ = .148)
Sad as neutral	15.80	15.27	12.41	9.67	−0.637	.524
Neutral as happy	23.49	14.45	21.39	13.49	−0.667	.505
Neutral as sad	40.52	13.91	41.67	11.31	−0.396	.692

[a]Significance is not retained after Bonferroni correction for multiple testing.
Abbreviations: CATS = Comprehensive Affective Testing System, 1 = subtest 9, 2 = subtest 10.
Symbols: ↑ = significantly higher than in the control group, $P < .05$; (↑) = higher than in the control group at a trend level, $P < .10$; (↓) = lower than in the control group at a trend level, $P < .10$.

Table 3. Quality of Life Scores According to the WHOQOL-BREF[a] (Mean ± SD)

	Group		Mann-Whitney *U* Test
Domain	Patients	Controls	*P* Value
Physical health	65.7 ± 16.6	90.2 ± 9.4	< .001
Psychological health	64.5 ± 18.0	82.6 ± 9.5	< .001
Social relationships	65.1 ± 20.0	82.6 ± 13.5	< .001
Environment	75.3 ± 15.1	84.2 ± 10.3	< .001
Global quality of life	65.3 ± 20.8	86.4 ± 10.6	< .001

[a]Range: 0 (poorest quality of life) to 100 (best quality of life).
Abbreviations: WHOQOL-BREF = World Health Organization quality of life, abbreviated version

Association of prosodic and semantic affect perception with patient outcomes. The correlations of CATS 1 performance and patients' symptomatic and functional outcomes are summarized in Table 4. Poorer identification of emotions expressed by the voice (CATS 1: total score; happy and neutral prosody) as well as misinterpretations toward a more negative emotionality (ie, happy misinterpreted as neutral or sad) were significantly associated with higher scores on the MADRS. Note, however, that none of these correlations remained significant after Bonferroni correction. Correlations of CATS 1 performance and the YMRS did not reach statistical significance.

With regard to functional outcomes, a better performance on the CATS 1 (total score; happy, sad, and neutral prosody) was positively associated with patients' overall level of functioning (GAF) and with their employment status: patients with regular paid work scored significantly higher than those without. Concerning misinterpretations, lower GAF scores were significantly associated with more misattributions both toward a more negative emotionality and toward a more positive emotionality. Similar findings were obtained regarding patients' employment status (unemployment went along with a higher rate of misinterpretations in either direction). Most of the correlations of CATS 1 and functional outcome remained significant after Bonferroni correction. There were no significant correlations between CATS 1 performance and patients' partnership status or living situation.

The CATS 2 total score was positively correlated with the GAF score ($P = .008$, $P_{Bonferroni} = .032$). No other correlation between CATS 2 total score or subscores and symptomatic or functional outcomes reached statistical significance.

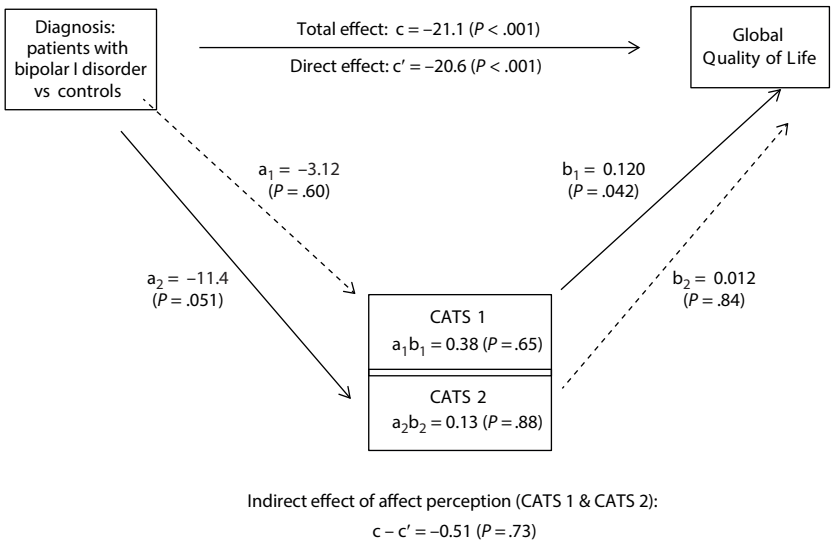
The CATS 1 total score showed a positive correlation with global QoL ($r = 0.29$, $P = .029$) and also with the subdomains of physical ($r = 0.31$, $P = .018$) and psychological QoL ($r = 0.34$, $P = .010$). However, only the correlation with psychological QoL remained significant after Bonferroni correction ($P_{Bonferroni} = .049$). There were no significant correlations between the CATS 2 total score and any QoL domains.

Table 4. Correlation of CATS 1 With Symptomatic and Functional Outcomes of Bipolar Patients

		Symptomatic Outcome		Functional Outcome	
		MADRS	YMRS	GAF	Employment (yes/no)[a]
Total score	$r_{Spearman}$	−0.263*	−0.194	0.433**	0.426**
	P	.046	.144	.001	.001
	$P_{Bonferroni}$	.184	.576	.004	.004
Individual emotions					
Happy, % correct	$r_{Spearman}$	−0.288*	0.032	0.343*	0.348*
	P	.028	.813	.009	.009
	$P_{Bonferroni}$	336	1.000	.108	.108
Sad, % correct	$r_{Spearman}$	−0.028	−0.197	0.308*	0.405**
	P	.832	.139	.020	.002
	$P_{Bonferroni}$	1.000	1.000	.240	.024
Neutral, % correct	$r_{Spearman}$	−0.323*	−0.201	0.420**	0.332*
	P	.013	.130	.001	.012
	$P_{Bonferroni}$	.156	1.000	.012	.144
Misinterpretations (summarized)					
Toward a more negative emotionality,[b] %	$r_{Spearman}$	0.328*	0.111	−0.401**	−0.362**
	P	.012	.405	.002	.006
	$P_{Bonferroni}$	.096	1.000	.016	.048
Toward a more positive emotionality,[c] %	$r_{Spearman}$	0.058	0.193	−0.310*	−0.427**
	P	.663	.147	.019	.001
	$P_{Bonferroni}$	1.000	1.000	.152	.008

[a]The point-biserial correlation coefficient, r_{pb}, rather than $r_{Spearman}$, was used for correlations involving the dichotomous variable employment (yes/no).
[b]Happy misinterpreted as neutral or sad, or neutral misinterpreted as sad.
[c]Sad misinterpreted as neutral or happy, or neutral misinterpreted as happy.
*$P < .05$.
**$P_{Bonferroni} < .05$.
Abbreviations: GAF = Global Assessment of Functioning Scale, MADRS = Montgomery-Asberg Depression Rating Scale, YMRS = Young Mania Rating Scale.

Figure 1. Indirect Effect of Prosodic (CATS 1) and Semantic (CATS 2) Affect Perception on the Relationship Between Diagnosis and Global Quality of Life: Results of Multiple Mediation Analysis[a]



[a]Numbers shown are unstandardized regression coefficients. Solid lines indicate statistically significant effects (including 1 nearly significant P value of .051); dashed lines indicate nonsignificant effects. The coefficients a_1 and a_2 represent the effect of the diagnosis on the mediators CATS 1 and CATS 2, respectively; b_1 and b_2 represent the effect of CATS 1 and CATS 2, respectively, on global quality of life; a_1b_1 is the product of a_1 and b_1 and represents the indirect effect of the mediator CATS 1 on the relationship between diagnosis and global quality of life (accordingly for a_2b_2).
Abbreviation: CATS = Comprehensive Affective Testing System, 1 = subtest 9, 2 = subtest 10.

Investigation of prosodic affect perception and semantic affect perception as potential mediators between group and QoL. In order to analyze the association between group prosodic/semantic affect perception and QoL in more detail, we performed a multiple mediation analysis, as shown in Figure 1. Our aim was to investigate whether the large difference in QoL between patients with bipolar disorder and healthy controls (65.3 vs 86.4 points, respectively, resulting in a difference of c = 21.1 points [total effect]) can at least be explained in part by differences in prosodic and/or semantic affect perception between the 2 groups. Multiple mediation analysis revealed that neither prosodic (CATS 1) nor semantic (CATS 2) affect perception significantly mediated the association between group and QoL. Overall, the indirect effect of group on QoL, via the path "group" → "affect perception" → "QoL," amounted to 0.51 points on the QoL scale, ie, it was very small compared to the total effect of 21.1 points and did not attain statistical significance ($P = .73$). There remained a large, highly significant QoL difference of 20.6 points between the 2 groups not attributable to prosodic or semantic affect perception (direct effect). Findings of the mediation analyses for the other subscales of the WHOQOL-BREF were similar. No significant mediation effects were found.

DISCUSSION

The present study was conducted to examine prosodic and semantic affect perception in patients with bipolar disorder in remission. To this end, subjects were asked to listen to affect-laden sentences and to focus either on the prosody while ignoring the affective meaning (CATS 1) or inversely on the affective meaning while ignoring the prosody (CATS 2).

In general, bipolar disorder has consistently been associated with deficits in the recognition, discrimination, and experience of emotional stimuli.[3] In the current study, patients were found to perform similarly to healthy controls when focusing on the vocal emotion while ignoring the affective meaning of test trials (CATS 1), but they showed some impairment in the perception of the affective meaning of test trials when ignoring the vocal emotion (CATS 2).

Accordingly, in remitted patients with bipolar disorder, prosodic affect perception seems to be less impaired than semantic affect perception. These deficits may indicate right hemisphere impairments[26]; however, this has to be investigated in functional imaging studies.

Our finding of intact prosodic affect perception corroborates that of Vaskinn et al[8] but is partially opposite to that of Bozikas et al,[9] who found some deficits in this area. However, the impairment reported in that study was specific to a small sample of female patients and to certain emotions. In view of our previous findings on facial emotion recognition abilities,[11] the current results, as well as those of Vaskinn et al,[8] suggest that in remitted patients with bipolar disorder, prosodic affect perception is less impaired than both semantic affect perception and the recognition of facial emotions. Further studies are needed to investigate patients' ability to connect different communication channels (eg, facial + prosodic intonational).

Comparable to previous observations in major depressive disorder,[5] both healthy controls and symptomatically remitted patients with bipolar disorder profited likewise from the congruence of prosody and affective meaning. This may be seen as an indirect indicator of intact executive functioning. However, we did not assess basic neurocognition, and previous studies suggest that euthymic patients with bipolar disorder may be significantly impaired in this domain.[27] This assumption clearly calls for longitudinal studies investigating both prosodic and semantic affect perception and neurocognitive functioning during both mood episodes and periods of remission.

Interestingly, patients frequently misinterpreted sadly expressed emotions as happy ones in both tasks. Although we detected merely narrow differences concerning these misinterpretations, and these findings did not withstand Bonferroni correction for multiple testing, it has to be emphasized that this is the first study investigating misinterpretations of prosodic and semantic affect perception in remitted patients with bipolar disorder. Generally, during depressed states, patients are known to be impaired in the recognition of positive emotions,[4,28] whereas manic patients are said to be especially impaired in recognizing negative emotions.[29] In addition, studies using the emotional Stroop task have shown that patients are slower to name the color of a word associated with concerns relevant to their clinical condition.[30] However, these considerations cannot be translated to our sample since our patients were symptomatically remitted at the time of study inclusion. In accordance with Mikhailova et al,[31] we, therefore, suggest that impairments in the recognition of sadness may reflect a defensive brain mechanism that prevents subjects from realizing unpleasant stimuli, which may destabilize patients suffering from bipolar disorder. However, the origin and meaning of this effect remain unclear.

In both patients and controls, we detected a small gender difference regarding the recognition of neutral prosody favoring male participants. Generally, men and women appear to differ in the manner in which they perceive, process, express, and experience emotions. There is evidence for marked sex differences in the neural mechanisms underlying emotional processes with higher limbic/subcortical and temporal brain activation in females and higher frontoparietal brain activation in males.[32] On the whole, females tend to be more emotionally expressive than males, and the 2 sexes show differences in their responsiveness to affectively charged stimuli.[33,34] In addition, females tend to rate their emotions more intensely,[35] are more accurate in perceiving facial expressions,[36] and demonstrate greater ease at decoding nonverbal messages than males.[37] However, in view of our findings, they may also be prone to misconceive neutral prosody, which could potentially result in difficulties in communication.

Despite being symptomatically remitted, patients who had relatively higher total scores on the MADRS were impaired in prosodic affect perception (CATS 1) and frequently exhibited misinterpretations toward a more negative emotionality (happy prosody perceived as neutral and neutral prosody as sad). Accordingly, even a mild degree of depressive symptoms may have a negative impact on prosodic affect perception. This observation corresponds to that of previous studies.[4,6,7] Clearly, a hyperthymic temperament or residual hypomanic symptomatology may color a patient's affect perception. Unfortunately, we did not assess temperament; however, as the patients included into the study were symptomatically remitted and reached a very low mean YMRS score, we can rule out a potential impact of hypomanic symptoms on our findings.

Our findings of significant differences between patients and control subjects with regard to partnership and employment status, living situation, and QoL corroborate those of other studies.[11,38–42] However, we found no direct link between the large QoL differences and prosodic and semantic affect perception. One possible explanation for this might be that a person's QoL is affected by such a large number of demographic, functional, clinical, and other factors that the contribution of affect perception alone was too small to have a direct effect on QoL.

Obviously, deficits in prosodic and semantic affect perception contribute to functional impairments. In addition, residual symptoms of bipolar disorder,[42] the psychosocial consequences of behavioral disturbances during manic episodes, as well as those following depressive states, and the mean duration of illness of over 13 years are quite likely to have contributed to psychosocial impairments in our sample, and thus, to reduced QoL. This clearly emphasizes the necessity to offer continuous medical and psychosocial care, even when patients are in remission. In the context of the latter, we suggest that difficulties in semantic affect perception may represent a target for psychotherapeutic interventions that include the strengthening of skills to detect and communicate emotions.

The current study has some limitations. First, we have not tested hearing ability, and we have not investigated the potential influence of medication on the outcomes studied. Antidepressants, for instance, have been demonstrated to

differentially modulate emotion-processing brain regions,[43] and antipsychotic treatment has been associated with small improvements in emotion perception in patients with schizophrenia.[44] However, as all patients were symptomatically remitted, we can at least disregard efficacy differences between the different drugs. Clearly, adverse events, such as sedation, may have an impact on the reported results. Second, the YMRS and MADRS remission criteria were applied cross-sectionally, and we did not register when patients first met these criteria. Therefore, patients may have experienced different durations of clinical stability, potentially affecting course of illness and psychosocial outcomes. Third, we have not determined former psychotherapeutic or psychosocial interventions in patients, which may impact affect perception abilities. In addition, participants' neurocognitive functioning, which clearly may interfere with affect recognition abilities, was not tested. Finally, although we have found substantial correlations between different outcome measures, the design of the current study does not allow for direct causal conclusions regarding the influence of symptomatic remission and prosodic and semantic affect perception on patients' outcomes. As this was a cross-sectional study, it will be critical to generate longitudinal follow-up data to determine how the associations of these determinants interact and change over time. In addition, future research is needed to explore the impact of pharmacologic and psychosocial interventions on prosodic and semantic affect perception, even when patients are in symptomatic remission.

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