



Research paper

Quality of life in stabilized outpatients with bipolar I disorder: Associations with resilience, internalized stigma, and residual symptoms



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ABSTRACT

Objectives: Improving Quality of Life (QoL) is an important objective in the treatment of bipolar disorder. The aim of the current study was to examine to which extent resilience, internalized stigma, and psychopathology are correlated to QoL.

Methods: We recruited 60 outpatients diagnosed with bipolar I disorder according to DSM-IV criteria and 77 healthy control subjects from the general community. In patients, symptoms were quantified by the Montgomery-Åsberg Depression Rating Scale (MADRS) and the Young Mania Rating Scale (YMRS) and internalized stigma by the Internalized Stigma of Mental Illness (ISMI) scale. In order to assess QoL and resilience, the Berliner Lebensqualitätsprofil (BELP) and the Resilience Scale (RS-25) were used in both patients and control subjects.

Results: Despite presenting with a very mild symptom level and relatively low internalized stigma, patients with bipolar I disorder indicated significantly lower QoL and resilience as compared to healthy control subjects. In patients, QoL correlated significantly with resilience, internalized stigma, and residual symptoms of depression. No significant correlations were observed between QoL and residual manic symptoms.

Limitations: The cross-sectional design and the relatively small sample size limit the generalizability of our results. Furthermore, levels of resilience and internalized stigma may change over the course of the illness and have different impacts on the long-term outcome of patients with bipolar disorder.

Conclusion: Our results show that QoL of patients suffering from bipolar I disorder, even when only mildly ill, is strongly associated with the degree of resilience and internalized stigma, and that particularly residual depressive symptoms have a negative impact on QoL. In addition to drug treatment, psychotherapeutic approaches should be applied to strengthen resilience, to reduce internalized stigma, and, ultimately, to improve quality of life.

1. Introduction

Bipolar disorder (BD) imposes a huge burden upon patients and leads to decreased quality of life (QoL) (Dean et al., 2004), even during periods of clinical remission (Arnold et al., 2000). First and foremost, depressive symptoms of the illness have been associated with significant psychosocial impairment (Bauwens et al., 1991; Calabrese et al., 2003; Coryell et al., 1993; MacQueen et al., 2001), which, in turn, has a negative impact on patients' quality of life (Robb et al., 1997; Vojta et al., 2001).

Next to the mental illness by itself, internalized stigma, i.e., the

inner subjective experience of stigma resulting from applying negative stereotypes and stigmatizing attitudes to oneself, adds to the burden (Ellison et al., 2013; Hawke et al., 2013; Ritsher et al., 2003) and leads to lower self-esteem, social impairment, and lower levels of functioning (Hawke et al., 2013), which again may worsen quality of life (Hawke et al., 2014). Of note, internalized stigma also negatively influences adherence (Hawke et al., 2013).

There is growing interest in the effects of resilience in psychiatric illnesses. Resilience can be defined as “the capacity of a dynamic system to withstand or recover from significant challenges that threaten its stability, viability or development” (Masten, 2011). A high degree of

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resilience has been shown to reduce the risk of suicide in depression (Nruugham et al., 2010) and to have a positive impact on the long-term outcome in schizophrenia (Torgalsboen, 2012). In their study investigating resilience and impulsivity in bipolar patients, Choi et al. (2015) found that low levels of resilience were associated with an increased number of depressive episodes and high levels of impulsivity. However, research on the role of resilience in bipolar disorder is rather scarce.

We have recently shown that a higher degree of resilience is associated with better quality of life (Mizuno et al., 2016; Wartelsteiner et al., 2016) and a lower degree of internalized stigma (Hofer et al., 2016) in patients with schizophrenia. We also found lower QoL and resilience scores in patients suffering from bipolar I disorder (BD-I) compared to healthy control subjects (Hofer et al., 2017), which is similar to the findings of Lee and colleagues (Lee et al., 2017). The latter were, to the best of our knowledge, the first group investigating the effects of resilience on quality of life in patients with bipolar disorder. However, they did not investigate the joint effects of psychopathology and internalized stigma which are known to have an impact upon quality of life. To fill this gap, the primary objective of the current study was to investigate the impact of resilience, internalized stigma, and residual symptoms on quality of life in clinically stable outpatients suffering from BD-I.

2. Patients and methods

The study sample consisted of patients suffering from BD-I aged between 18 and 65 years, who were recruited from the outpatient clinic of the Department of Psychiatry, Psychotherapy and Psychosomatics of the Medical University Innsbruck and of healthy control subjects recruited from the general community. Both patients and healthy controls had to be native German speakers. Patients and control subjects were comparable regarding age, sex and education. The Mini International Neuropsychiatric Interview (M.I.N.I.) (Sheehan et al., 1998) was used to confirm diagnosis in patients and to exclude any axis I disorder according to DSM-IV in control subjects. At the time of study inclusion, patients had to be clinically stable for at least six months, i.e., they had to be treated as outpatients without any modification of the treatment regimen. A brief medical screening interview was used in both patients and healthy controls to exclude subjects with any physical or neurological illness or any condition affecting neural or cerebrovascular function. The study was approved by the local ethics committee and all participants provided written informed consent.

Quality of life was assessed by the Berliner Lebensqualitätsprofil (BELP) (Priebe et al., 1995), which is the German version of the Lancashire Quality of Life Profile (Oliver et al., 1997). The translation of this scale and its validity properties have been shown to be satisfactory (Cronbach's $\alpha = 0.88$ for overall QoL and 0.93 for all subscales together) (Kaiser et al., 1996). The questionnaire includes nine domains: work/occupation, leisure time, financial situation, housing, personal safety, family life, friends, physical health, and mental health. Items are scored on a 7-score item scale with a score of 1 indicating "poorest quality of life", and a score of 7 "optimal quality of life".

Resilience was measured using the German translation (Schumacher et al., 2005) of the Resilience Scale (RS-25), (Wagnild and Young, 1993) which is the only resilience scale validated in German. The authors of the RS-25 conceptualized resilience as "a positive personality characteristic that enhances individual adaption" (Wagnild and Young, 1993). It consists of 25 items divided into two categories: "acceptance of self and life" (8 items) and "personal competence" (17 items). The subscale "acceptance of self and life" highlights features such as adaptability, tolerance, flexibility, and balance, whereas the subscale "personal competence" summarizes features such as self-reliance, independence, determination, mastery, perseverance, invincibility and resourcefulness. Since the 2-factor structure could not be identified in the German version (Schumacher et al., 2005), we

considered only the total score for our study (Cronbach's $\alpha = 0.95$). All items are scored on a 7-score item scale, ranging from 1 = strongly disagree to 7 = strongly agree with possible scores ranging from 25 to 175. The overall RS-25 score is categorized into 3 levels: scores below 125 reflect low resilience, scores between 126 and 145 indicate moderately low to moderate levels of resilience, and scores of 146 and higher indicate high resilience (Wagnild, 2009).

In patients, internalized stigma was assessed by the Internalized Stigma of Mental Illness (ISMI) scale (Ritsher et al., 2003), which consists of 29 items and uses a Likert-scale from 1 = strongly disagree to 4 = strongly agree. The scale itself is composed of five subscales: alienation (6 items), stereotype endorsement (7 items), discrimination experience (5 items), social withdrawal (6 items), and stigma resistance (5 items). Scores range from: 29 (no internalized stigma) to 116 (high internalized stigma). Furthermore, a mean score of all items of the ISMI can be calculated, which ranges from 1–4. The five "stigma resistance" items are reverse-coded and serve as a validity check. The extent of internalized stigma and its subscales has previously been defined using a cut-off point of 2.5 on the mean item scores. Accordingly, a value of 2.5 and above can be applied to define moderate to high internalized stigma and less than 2.5 for low internalized stigma (Lau et al., 2017).

In patients, the presence and severity of depression or mania were measured by the Montgomery-Åsberg Depression Rating Scale (MADRS) (Montgomery and Åsberg, 1979) and the Young Mania Rating Scale (YMRS) (Young et al., 1978), respectively. The MADRS consists of 10 items (apparent sadness, reported sadness, inner tension, reduced sleep, reduced appetite, concentration difficulties, lassitude, inability to feel, pessimistic thoughts, and suicidal thoughts) and each item yields a score of 0 to 6. The overall score ranges from 0 to 60 with higher scores reflecting more severe depression. The YMRS consists of 11 items with scores ranging from 0 to 4 or 8 according to item: elevated mood (score 0 = absent to 4 = euphoric), increased motor activity (score 0 = absent to 4 = motor excitement), sexual interest (score 0 = normal to 4 = overt sexual acts), sleep (score 0 = no decrease in sleep to 4 = denies need for sleep), irritability (score 0 = absent to 8 = hostile, uncooperative), speech (score 0 = no increase to 8 = pressured, uninterruptible), thought disorder/language (score 0 = absent to 4 = incoherent), content (score 0 = normal to 8 = delusions, hallucinations), disruptive-aggressive behavior (score 0 = absent, cooperative to 8 = assaultive, destructive), appearance (score 0 = appropriate to 4 = completely unkempt, decorated, bizarre garb), and insight (score 0 = present to 4 = denies any behavior changes). The overall score ranges from 0 to 60. Both the MADRS and the YMRS are validated in their German versions (Maier and Philipp, 1985; Muhlbacher et al., 2011) (Cronbach's $\alpha = 0.74$ and 0.86, respectively).

Except for the MADRS and YMRS which are clinician-rated, all scales are self-rated.

3. Statistical methods

Prior to the analysis, numeric variables were tested for deviations from a normal distribution by means of the Shapiro-Wilk test. The *t*-test, Mann-Whitney U-test and Chi-square test were applied to compare patients and control subjects with regard to sociodemographic variables, depending on the variable type (normally distributed, non-normally distributed, and categorical, respectively). Group comparisons with respect to QoL data were performed by means of the Mann-Whitney U-test as the distribution of most of the BELP subscales showed significant deviations from normality. In the patient group, the relationship between QoL and resilience, internalized stigma, and psychopathology was investigated by means of non-parametric correlation analysis (Spearman rank correlation coefficient). In addition, the joint effect of sociodemographics (age, sex, and education), symptoms, and psychological scales (RS-25, ISMI) on QoL was investigated by means of multiple linear regression. Both overall QoL and QoL subscales were considered as dependent variables. QoL subscales with a non-normal

distribution were subjected to a square root transformation prior to the analysis. The forward stepwise selection method was used to identify significant predictors of QoL (a second analysis with stepwise backward variable elimination yielded the same results). As a measure of determination of the regression model, R^2 was reported. All statistical tests were performed at a 0.05 level of significance.

4. Power analysis

The following power analysis was performed using gPower, version 3.1.7, assuming a type-I-error of 0.05 and a power of 0.8 throughout. The sample size of 60 BD-I patients and 77 control subjects used in the study was sufficiently large to detect, by Mann-Whitney U-test, group differences exceeding an effect size of $d = 0.5$ (or $d = 0.49$ for comparisons by t -test) (Cohen, 1992). Moreover, a sample size of 60 BD-I patients allows detection of associations between numeric variables by Spearman-rank correlation if the correlation coefficient, ρ , is ≥ 0.355 . This is a medium correlation according to Cohen's classification. Finally, in a multiple linear regression analysis with up to 7 predictors, a sample size of 60 is sufficiently large to detect statistical significance of an individual predictor if its effect size exceeds a Cohen f^2 of 0.136, which is again a medium effect size.

5. Results

5.1. Sociodemographic and clinical characteristics

Table 1 summarizes sociodemographic and clinical data of both patients and healthy control subjects. We recruited 77 healthy control subjects and 60 patients suffering from BD-I. Patients had a mean age of 42.9 ± 11.1 (mean \pm standard deviation) years, a mean duration of illness of 11.6 ± 10.2 years, and very mild residual symptoms (MADRS score: 7.41 ± 8.23 , YMRS score: 1.44 ± 2.84). Most of them received

Table 1
Sociodemographic and clinical data.

Variable	Group		Comparison	
	Bipolar patients (N = 60)	Control subjects (N = 77)	Statistic	p-value
Age	42.9 \pm 11.1	42.8 \pm 12.1	t = 0.09	0.739
Sex				
Male	25 (42%)	27 (35%)	$\chi^2 = 0.23$	0.634
Female	35 (58%)	50 (65%)		
Education (years)	13.7 \pm 3.2	13.8 \pm 3.4	Z = -0.16	0.876
Duration of illness (years)	11.6 \pm 10.2	-		
Resilience (RS-25)	129.8 \pm 23.1	150.4 \pm 14.2	Z = -4.92	<0.001
MADRS	7.41 \pm 8.23	-		
YMRS	1.44 \pm 2.84	-		
ISMI				
Sum score	55.2 \pm 16.6	-		
Mean score	1.90 \pm 0.57	-		
Treatment, N (%)				
MS mono-therapy	10 (17)			
AP mono-therapy	3 (5)			
AD mono-therapy	5 (8)			
MS + AP	16 (27)			
MS + AD	5 (8)			
AP + AD	2 (3)			
MS + AP + AD	13 (22)			
No medication	6 (10)			

Values are shown as mean \pm standard deviation or N (%)
RS-25 = Resilience Scale, MADRS = Montgomery-Asberg Depression Rating Scale, YMRS = Young Mania Rating Scale, ISMI = Internalized Stigma of Mental Illness scale, MS = mood stabilizer, AP = antipsychotic, AD = antidepressant.

Table 2
Quality of life in bipolar patients and control subjects.

BELP subscale (range 1–7) ^a	Group		Comparison ^b	
	Bipolar patients (N = 60)	Control subjects (N = 77)	Effect size, d	p-value
Overall QoL	4.59 \pm 1.61 ↓	6.01 \pm 0.82	-1.18	<0.001
Work/occupation	4.53 \pm 1.55 ↓	5.22 \pm 1.31	-0.49	0.007
Leisure time	4.65 \pm 1.53 ↓	5.50 \pm 0.98	-0.69	0.001
Financial situation	4.25 \pm 1.70 ↓	5.20 \pm 1.29	-0.65	0.002
Housing	5.51 \pm 1.24	6.07 \pm 1.08	-0.49	0.139
Safety	6.34 \pm 0.99	6.25 \pm 0.71	0.11	0.515
Family	5.45 \pm 1.31 ↓	6.12 \pm 0.90	-0.62	<0.001
Friends	5.25 \pm 1.28 ↓	6.27 \pm 0.64	-1.07	<0.001
Physical health	5.13 \pm 1.33 ↓	5.66 \pm 1.18	-0.42	0.013
Mental health	4.41 \pm 1.74 ↓	6.35 \pm 0.74	-1.56	<0.001

Values are shown as mean \pm standard deviation
BELP = Berliner Lebensqualitätsprofil, QoL = quality of life.
↓ Significantly lower than in the control group.

^a 1 = poorest quality of life, 7 = optimal quality of life

^b Mann-Whitney U test.

combined psychopharmacological treatments. They presented with a relatively low ISMI sum score (55.2 ± 16.6) and a relatively high stigma resistance mean score. Resilience level was significantly lower in patients compared to healthy individuals (129.8 ± 23.1 vs. 150.4 ± 14.2).

5.2. Quality of life

Compared to control subjects, patients suffering from BD-I indicated lower overall QoL and less satisfaction on all life domains assessed by the BELP (see Table 2), except for the subscale safety whose mean value was slightly higher in patients than healthy controls. Statistical significance was achieved for all subscales, except for housing and safety. In patients, the subscale safety received the highest satisfaction rating, while the subscale mental health was rated lowest. Control subjects, in turn, scored highest for the subscale mental health and lowest for the subscale financial situation.

5.3. Association of patients' quality of life with resilience, internalized stigma, and symptoms

Correlations of patients' QoL with resilience, internalized stigma, and residual symptoms are presented in Table 3. Positive and

Table 3
Correlation of bipolar patients' quality of life with resilience, internalized stigma, and psychopathology.

BELP subscale	RS-25	ISMI total	MADRS	YMRS
Overall QoL	0.680**	-0.588**	-0.655**	0.061
Work/occupation	0.297*	-0.436**	-0.357**	-0.037
Leisure time	0.604**	-0.646**	-0.541**	0.136
Financial situation	0.215	-0.175	-0.237	0.010
Housing	0.144	-0.217	-0.114	-0.123
Safety	0.115	-0.208	-0.210	-0.025
Family	0.205	-0.331*	-0.259*	-0.054
Friends	0.469**	-0.492**	-0.487**	-0.121
Physical health	0.446**	-0.459**	-0.541**	-0.114
Mental health	0.441**	-0.510**	-0.589**	0.024

Spearman rank correlation coefficient.
BELP = Berliner Lebensqualitätsprofil, RS-25 = Resilience Scale, ISMI = Internalized Stigma of Mental Illness Scale, MADRS = Montgomery-Asberg Depression Rating Scale, YMRS = Young Mania Rating Scale, QoL = quality of life
^{*} $p < 0.05$, ^{**} $p < 0.01$, otherwise $p > 0.10$.

Table 4
Predictors of BERP overall quality of life and BERP subscores in bipolar patients - findings of multiple linear regression analysis.

Dependent variable	R ² adjusted	Independent variables		
		Sociodemographics	Psychopathology (MADRS, YMRS)	Psychological scales (RS-25, ISMI)
Overall QoL	0.557	–	MADRS: $\beta = -0.438^{***}$	RS-25: $\beta = 0.406^{**}$
Work/occupation	0.227	–	–	ISMI: $\beta = -0.491^{***}$
Leisure time	0.560	Age: $\beta = -0.247^{**}$	MADRS: $\beta = -0.226^*$	RS-25: $\beta = 0.273^*$; ISMI: $\beta = -0.313^*$
Financial situation	0.000	–	–	–
Housing ^a	0.000	–	–	–
Safety ^a	0.000	–	–	–
Family ^a	0.096	Education: $\beta = -0.260^*$	–	ISMI: $\beta = -0.333^*$
Friends ^a	0.303	Age: $\beta = -0.290^*$	–	RS-25: $\beta = 0.493^{***}$
Physical health ^a	0.250	Age: $\beta = -0.310^*$	–	RS-25: $\beta = 0.425^{**}$
Mental health	0.328	–	MADRS: $\beta = -0.342^*$	ISMI: $\beta = -0.338^*$

R² = coefficient of determination

β = standardized regression coefficient

BERP = Berliner Lebensqualitätsprofil, QoL = quality of life, RS-25 = Resilience Scale, ISMI = Internalized Stigma of Mental Illness Scale, MADRS = Montgomery-Asberg Depression Rating Scale, YMRS = Young Mania Rating Scale

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

^a Square-root transformation to obtain approximately normal distribution of dependent variable.

significant correlations were found between resilience and the BERP-subscores overall QoL, work/occupation, leisure time, friends, physical health, and mental health. Negative correlations were found between the ISMI total score and the BERP-subscores overall QoL, work/occupation, leisure time, family, friends, physical health, and mental health. Residual depressive symptoms captured by the MADRS negatively correlated with overall QoL and the BERP-subscores work/occupation, leisure time, family, friends as well as physical and mental health, while no significant relationship was found between QoL and residual manic symptoms.

5.4. Prediction of patients' quality of life by sociodemographics, resilience, internalized stigma, and symptoms: results of regression analysis

The joint effect of sociodemographics, symptoms and psychological scales on patients' QoL was investigated by multiple regression analysis (see Table 4). Both residual depressive symptoms and resilience emerged as significant predictors of overall QoL (the former being associated with poorer QoL, the latter with higher QoL). Depression was also observed as a significant predictor of lower QoL in the areas of leisure time and mental health. Resilience predicted higher QoL scores in leisure time activities, social activities (friends), and physical health. Internalized stigma emerged as a predictor of lower QoL in the areas of work/occupation, leisure time, and mental health. Of the socio-demographic variables, higher age predicted lower QoL scores in the areas of physical health, friends, and leisure time activities, whereas higher levels of education were associated with poorer QoL in family life.

None of the potential predictors investigated showed a significant effect on patients' QoL in the areas of finances, housing, or safety.

6. Discussion

To the best of our knowledge, up to date only one study (Lee et al., 2017) has investigated the relationship between QoL and resilience in patients suffering from bipolar disorder. However, they did not assess the effects of internalized stigma and residual symptoms, two important aspects which have been shown to impact upon QoL in previous studies (Bauwens et al., 1991; Calabrese et al., 2003; Coryell et al., 1993; Hawke et al., 2014; MacQueen et al., 2001; Masten, 2011; Robb et al., 1997; Vojta et al., 2001). In this study, we recruited a group of chronically ill patients from our specialized outpatient clinic with a low level of symptoms, as shown by sociodemographic data and MADRS and YMRS scores. On the one hand, this approach targets a group of

patients one is interested in when evaluating long term management, on the other hand our findings cannot be generalized, implying that they should be interpreted cautiously.

Although it has been criticized that self-report of QoL may be influenced by the "mood bias" (Hirschfeld et al., 1983), past studies have shown that euthymic and depressed outpatients can provide reliable self-report on their QoL (Leidy et al., 1998) and we therefore do not expect that the affective symptoms have distorted our patients' reports of QoL given they were mildly ill at most. On the other hand, we cannot rule out that patients overestimated their quality of life to please their treating physician. Consistent with previous findings, patients were less satisfied with most aspects of their life than healthy control subjects (Lee et al., 2017; Sierra et al., 2005; Yatham et al., 2004; Yen et al., 2008), with residual depressive symptoms being of major relevance in this context (Michalak et al., 2005; Yalcin-Siedentopf et al., 2014). When compared to control subjects, especially the BERP-subscores „Overall QoL“, „Friends“ and „Mental health“ are to be pointed out in this context, since effect sizes (d) of > 1 could be found.

Michalak et al. (2006) identified social support and mental health being two of the major determinants of QoL in bipolar disorder and the results of this qualitative study led to the development of a disorder specific quality of life scale (QoL.BD) (Michalak, 2010). This instrument covers a wide spectrum of factors which were found to impact upon QoL in an earlier study (Michalak et al., 2006). Its developers suggest implementing this scale in routine clinical practice, since it may help clinicians better understand patient progress and consequently may be beneficial in underpinning therapeutic alliance (Michalak, 2010). Unfortunately, this scale is not yet available in German language and could therefore not be used in this study. Nevertheless, the BERP scale in our study captures some features which are found in the QoL.BD. Notably, our results also show the areas mental health and social support to be of central importance with regards to QoL.

Our findings and those of past studies, support the notion that patients suffering from BD-I, even when considered as remitted or those only experiencing residual symptoms, are in need for continuous psychosocial support. A review of literature regarding psychosocial therapy in bipolar disorder, has indicated a long-lasting prophylactic effect of group psychoeducation for patients in remission, and a positive effect of cognitive behavioral therapy (CBT) with booster sessions, especially to prevent depression (Reinares et al., 2014). Patients are more likely to benefit from both psychoeducation and CBT (Scott et al., 2013) in early stages of the illness, whereas chronically ill patients, such as patients included in the current study, may benefit more from acceptance-based interventions (Berk et al., 2014). Therefore, in the

context of personalized medicine and depending on availability, psychosocial interventions should be offered to all patients as soon as possible (Reinares et al., 2014).

Similar to the findings of Lee et al. (2017), lower resilience scores were found in patients with bipolar disorder compared to healthy control subjects. This was also found in patients with depressive disorder (Kesebir et al., 2013) and in patients with schizophrenia (Mizuno et al., 2016; Wartelsteiner et al., 2016). We also replicated the findings by Lee et al. (2017) showing a positive correlation between resilience and overall QoL as well as positive associations with all subdomains of QoL. Multiple linear regression analysis showed that resilience is a positive predictor for overall QoL. Psychosocial factors associated with resilience, such as optimism and active coping (Feder et al., 2009) may explain the positive associations found between resilience and QoL. Our findings indicate the relevance of resilience as a potential target for therapeutic intervention and future studies should investigate the efficacy of resiliency training programs for bipolar patients in terms of outcome.

As expected and similar to earlier findings (Livingston and Boyd, 2010; Michalak et al., 2006), we found a negative relationship between QoL and internalized stigma, showing that the less stigma a patient perceives, the better the QoL. In this study, a relatively low ISMI score was recorded, which may be explained by the relatively long mean duration of illness, thereby enabling our patients to develop coping strategies. Not only is internalized stigma a predictor of low psychosocial functioning (Cerit et al., 2012), it may also negatively influence treatment seeking behavior (Eisenberg et al., 2009) and treatment adherence (Livingston and Boyd, 2010) which in turn poses a major barrier to recovery (Yanos et al., 2008). In the current study, internalized stigma negatively predicted QoL in terms of work/occupation, leisure time, family, and mental health. Obviously, this emphasizes the need to reduce internalized stigma in patients by implementing anti-stigma interventions. In their review, Yanos et al. (2015) summarized that the available interventions aim to promote self-esteem, hope and self-efficacy and on the other hand decrease social avoidance. Since we have recently shown an association between self-esteem as well as hopelessness with resilience in patients with schizophrenia (Hofer et al., 2016), it may be possible that anti-stigma interventions can also have a positive effect on resilience, and this should be investigated in future studies.

The above mentioned review by Yanos et al. (2015) identified a number of anti-stigma interventions focusing on internalized stigma in mental illness, with all interventions using psychoeducation and most of them integrating cognitive techniques. These interventions showed promising effects, however, the authors argued that outcome and implementation is still in early stages. For bipolar disorder specifically we found a study by Cuhadar and Cam (2014) showing a positive effect of a psychoeducation program on levels of internalized stigma. Future studies are required to measure the impact of such interventions and should also investigate which interventions yield the best results for different patient groups (Yanos et al., 2015).

Altogether, our results show that internalized stigma is present in chronically ill and help-seeking patients, showing that this issue should be addressed throughout the course of illness. Although we only investigated internalized stigma in this study, structural and social stigma towards mental illnesses should not be disregarded, since they are also a serious concern for patients and their families (Hawke et al., 2013).

While quality of life measured by the BELP, as expected, negatively correlated with internalized stigma and residual depressive symptoms and positively with resilience, no significant associations were found between QoL and residual manic symptoms in our study, likely explained by a very low YMRS mean score. In contrast, yet investigating outpatients with a higher YMRS mean score, Gazalle et al. (2007) have shown manic symptoms to be related to poorer QoL. While we did not find any associations between sex and QoL, which corroborates the findings of Sierra and colleagues (Sierra et al., 2005) age and education

were negative predictors for some individual BELP-subcales. Similarly, two studies found age to be negatively correlated to individual QoL subcales (Chand et al., 2004; Cooke et al., 1996), whereas a third one did not report any correlations between age and QoL in bipolar patients (Robb et al., 1997). However, all studies used different scales to measure QoL and are therefore not easily comparable.

In summary, our results and those of previous studies highlight the complex nature of QoL in patients with bipolar disorder. Since both resilience and internalized stigma are correlated to quality of life, psychosocial and psychotherapeutic interventions should incorporate these two factors and should be part of a comprehensive therapy. Future longitudinal studies should investigate the impact of such interventions. Furthermore, continuous efforts should be made on a national/international level to reduce stigma towards the mentally ill.

7. Limitations

The cross-sectional design and the relatively small sample size limit the generalizability of our results. Patients experiencing acute symptoms or patients in an early stage of illness may have different levels of resilience and internalized stigma compared to more or less euthymic patients. We also did not record side effects of medication which are known to impact upon QoL (Yen et al., 2008). Furthermore, we did not use a disorder specific QoL scale and therefore may have failed to capture other important factors. With regard to resilience, the RS-25 scale only captures personal traits, while resilience is seen as a dynamic process, which calls for longitudinal quantitative studies. Furthermore, the levels of resilience and internalized stigma may change over the course of the illness and have different impacts on the long-term outcome of patients with bipolar disorder. Again, this should be assessed in a longitudinal fashion. Nevertheless, our results strongly suggest that resilience and internalized stigma play an important role in the long-term outcome of patients with bipolar disorder and should therefore not be disregarded in the treatment of patients.

Conflict of interest

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Declarations of interest

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References

- Arnold, L.M., Witzeman, K.A., Swank, M.L., McElroy, S.L., Keck Jr., P.E., 2000. Health-related quality of life using the SF-36 in patients with bipolar disorder compared with patients with chronic back pain and the general population. *J. Affect. Disord.* 57, 235–239.
- Bauwens, F., Tracy, A., Pardo, D., Vander Elst, M., Mendlewicz, J., 1991. Social adjustment of remitted bipolar and unipolar out-patients. A comparison with age- and sex-matched controls. *Br. J. Psychiatry* 159, 239–244.
- Berk, M., Berk, L., Dodd, S., Cotton, S., Macneil, C., Daglas, R., Conus, P., Bechdorf, A., Moylan, S., Malhi, G.S., 2014. Stage managing bipolar disorder. *Bipolar Disord.* 16, 471–477.
- Calabrese, J.R., Hirschfeld, R.M., Reed, M., Davies, M.A., Frye, M.A., Keck, P.E., Lewis, L., McElroy, S.L., McNulty, J.P., Wagner, K.D., 2003. Impact of bipolar disorder on a U.S. community sample. *J. Clin. Psychiatry* 64, 425–432.
- Cerit, C., Filizer, A., Tural, U., Tufan, A.E., 2012. Stigma: a core factor on predicting functionality in bipolar disorder. *Compr. Psychiatry* 53, 484–489.
- Chand, P.K., Mattoo, S.K., Sharan, P., 2004. Quality of life and its correlates in patients with bipolar disorder stabilized on lithium prophylaxis. *Psychiatry Clin. Neurosci.* 58, 311–318.
- Choi, J.W., Cha, B., Jang, J., Park, C.S., Kim, B.J., Lee, C.S., Lee, S.J., 2015. Resilience and

- impulsivity in euthymic patients with bipolar disorder. *J. Affect. Disord.* 170, 172–177.
- Cohen, J., 1992. A power primer. *Psychol. Bull.* 112, 155–159.
- Cooke, R.G., Robb, J.C., Young, L.T., Joffe, R.T., 1996. Well-being and functioning in patients with bipolar disorder assessed using the MOS 20-ITEM short form (SF-20). *J. Affect. Disord.* 39, 93–97.
- Coryell, W., Scheftner, W., Keller, M., Endicott, J., Maser, J., Klerman, G.L., 1993. The enduring psychosocial consequences of mania and depression. *Am. J. Psychiatry* 150, 720–727.
- Cuhadar, D., Cam, M.O., 2014. Effectiveness of psychoeducation in reducing internalized stigmatization in patients with bipolar disorder. *Arch. Psychiatr. Nurs.* 28, 62–66.
- Dean, B.B., Gerner, D., Gerner, R.H., 2004. A systematic review evaluating health-related quality of life, work impairment, and healthcare costs and utilization in bipolar disorder. *Curr. Med. Res. Opin.* 20, 139–154.
- Eisenberg, D., Downs, M.F., Golberstein, E., Zivin, K., 2009. Stigma and help seeking for mental health among college students. *Med. Care Res. Rev.* 66, 522–541.
- Ellison, N., Mason, O., Scior, K., 2013. Bipolar disorder and stigma: a systematic review of the literature. *J. Affect. Disord.* 151, 805–820.
- Feder, A., Nestler, E.J., Charney, D.S., 2009. Psychobiology and molecular genetics of resilience. *Nat. Rev. Neurosci.* 10, 446–457.
- Gazalle, F.K., Hallal, P.C., Andreazza, A.C., Frey, B.N., Kauer-Sant'Anna, M., Weyne, F., da Costa, S.C., Santin, A., Kapczynski, F., 2007. Manic symptoms and quality of life in bipolar disorder. *Psychiatry Res.* 153, 33–38.
- Hawke, L.D., Michalak, E.E., Maxwell, V., Parikh, S.V., 2014. Reducing stigma toward people with bipolar disorder: impact of a filmed theatrical intervention based on a personal narrative. *Int. J. Soc. Psychiatry* 60, 741–750.
- Hawke, L.D., Parikh, S.V., Michalak, E.E., 2013. Stigma and bipolar disorder: a review of the literature. *J. Affect. Disord.* 150, 181–191.
- Hirschfeld, R.M., Klerman, G.L., Clayton, P.J., Keller, M.B., McDonald-Scott, P., Larkin, B.H., 1983. Assessing personality: effects of the depressive state on trait measurement. *Am. J. Psychiatry* 140, 695–699.
- Hofer, A., Mizuno, Y., Frajo-Apor, B., Kemmler, G., Suzuki, T., Pardeller, S., Welte, A.S., Sondermann, C., Mimura, M., Wartelsteiner, F., Fleischhacker, W.W., Uchida, H., 2016. Resilience, internalized stigma, self-esteem, and hopelessness among people with schizophrenia: cultural comparison in Austria and Japan. *Schizophr. Res.* 171, 86–91.
- Hofer, A., Mizuno, Y., Wartelsteiner, F., Wolfgang Fleischhacker, W., Frajo-Apor, B., Kemmler, G., Mimura, M., Pardeller, S., Sondermann, C., Suzuki, T., Welte, A., Uchida, H., 2017. Quality of life in schizophrenia and bipolar disorder: The impact of symptomatic remission and resilience. *Eur. Psychiatry* 46, 42–47.
- Kaiser, W., Priebe, S., Hoffmann, K., Isermann, M., 1996. Subjektive Lebensqualität bei Patienten mit chronischer Schizophrenie. *Nervenarzt* 67, 572–582.
- Kesebir, S., Gundogar, D., Kucuksubasi, Y., Tatlidil Yaylaci, E., 2013. The relation between affective temperament and resilience in depression: a controlled study. *J. Affect. Disord.* 148, 352–356.
- Lau, Y.W., Picco, L., Pang, S., Jeyagurunathan, A., Satghare, P., Chong, S.A., Subramaniam, M., 2017. Stigma resistance and its association with internalised stigma and psychosocial outcomes among psychiatric outpatients. *Psychiatry Res.* 257, 72–78.
- Lee, D., Cha, B., Park, C.S., Kim, B.J., Lee, C.S., Lee, S.J., Seo, J.Y., Cho, Y.A., Ha, J.H., Choi, J.W., 2017. Effects of resilience on quality of life in patients with bipolar disorder. *J. Affect. Disord.* 207, 434–441.
- Leidy, N.K., Palmer, C., Murray, M., Robb, J., Revicki, D.A., 1998. Health-related quality of life assessment in euthymic and depressed patients with bipolar disorder. Psychometric performance of four self-report measures. *J. Affect. Disord.* 48, 207–214.
- Livingston, J.D., Boyd, J.E., 2010. Correlates and consequences of internalized stigma for people living with mental illness: a systematic review and meta-analysis. *Soc. Sci. Med.* 71, 2150–2161.
- MacQueen, G.M., Young, L.T., Joffe, R.T., 2001. A review of psychosocial outcome in patients with bipolar disorder. *Acta Psychiatr. Scand.* 103, 163–170.
- Maier, W., Philipp, M., 1985. Comparative analysis of observer depression scales. *Acta Psychiatr. Scand.* 72, 239–245.
- Masten, A.S., 2011. Resilience in children threatened by extreme adversity: frameworks for research, practice, and translational synergy. *Dev. Psychopathol.* 23, 493–506.
- Michalak, E.E., Murray, G., Collaborative Research Team to Study Psychosocial Issues in Bipolar Disorder (CREST.BD), 2010. Development of the QoL.BD: a disorder-specific scale to assess quality of life in bipolar disorder. *Bipolar Disord.* 12, 727–740.
- Michalak, E.E., Yatham, L.N., Kolesar, S., Lam, R.W., 2006. Bipolar disorder and quality of life: a patient-centered perspective. *Qual. Life Res.* 15, 25–37.
- Michalak, E.E., Yatham, L.N., Lam, R.W., 2005. Quality of life in bipolar disorder: a review of the literature. *Health Quality Life Outcomes* 3, 72.
- Mizuno, Y., Hofer, A., Suzuki, T., Frajo-Apor, B., Wartelsteiner, F., Kemmler, G., Saruta, J., Tsukinoki, K., Mimura, M., Fleischhacker, W.W., Uchida, H., 2016. Clinical and biological correlates of resilience in patients with schizophrenia and bipolar disorder: a cross-sectional study. *Schizophr. Res.* 175, 148–153.
- Montgomery, S.A., Asberg, M., 1979. A new depression scale designed to be sensitive to change. *Br. J. Psychiatry* 134, 382–389.
- Muhlbacher, M., Egger, C., Kaplan, P., Simhandl, C., Grunze, H., Geretsegger, C., Whitworth, A., Stuppach, C., 2011. Reliability and concordance validity of a German version of the Young Mania Rating Scale (YMRS-D). *Neuropsychiatr.* 25, 16–25.
- Nrugham, L., Holen, A., Sund, A.M., 2010. Associations between attempted suicide, violent life events, depressive symptoms, and resilience in adolescents and young adults. *J. Nerv. Ment. Dis.* 198, 131–136.
- Oliver, J.P., Huxley, P.J., Priebe, S., Kaiser, W., 1997. Measuring the quality of life of severely mentally ill people using the Lancashire Quality of Life Profile. *Soc. Psychiatry Psychiatr. Epidemiol.* 32, 76–83.
- Priebe, S., Gruyters, T., Heinze, M., Hoffmann, C., Jakel, A., 1995. [Subjective evaluation criteria in psychiatric care—methods of assessment for research and general practice]. *Psychiat. Prax.* 22, 140–144.
- Reinares, M., Sanchez-Moreno, J., Fountoulakis, K.N., 2014. Psychosocial interventions in bipolar disorder: what, for whom, and when. *J. Affect. Disord.* 156, 46–55.
- Ritscher, J.B., Otilingam, P.G., Grajales, M., 2003. Internalized stigma of mental illness: psychometric properties of a new measure. *Psychiatry Res.* 121, 31–49.
- Robb, J.C., Cooke, R.G., Devins, G.M., Young, L.T., Joffe, R.T., 1997. Quality of life and lifestyle disruption in euthymic bipolar disorder. *J. Psychiatr. Res.* 31, 509–517.
- Schumacher, J., Leppert, K., Gunzelmann, T., Strauß, B., Brähler, E., 2005. Die Resilienzskala-Ein Fragebogen zur Erfassung der psychischen Widerstandsfähigkeit als Personenmerkmal. *ZKPPP* 53, 16–39.
- Scott, J., Leboyer, M., Hickie, I., Berk, M., Kapczynski, F., Frank, E., Kupfer, D., McGorry, P., 2013. Clinical staging in psychiatry: a cross-cutting model of diagnosis with heuristic and practical value. *Br. J. Psychiatry* 202, 243–245.
- Sheehan, D.V., Lecrubier, Y., Sheehan, K.H., Amorim, P., Janavs, J., Weiller, E., Hergueta, T., Baker, R., Dunbar, G.C., 1998. The Mini-International Neuropsychiatric Interview (M.I.N.I.): the development and validation of a structured diagnostic psychiatric interview for DSM-IV and ICD-10. *J. Clin. Psychiatry* 59 (Suppl 20), 22–33 quiz 34–57.
- Sierra, P., Livianos, L., Rojo, L., 2005. Quality of life for patients with bipolar disorder: relationship with clinical and demographic variables. *Bipolar Disord.* 7, 159–165.
- Torgalsboen, A.K., 2012. Sustaining full recovery in schizophrenia after 15 years: does resilience matter? *Clin. Schizophr. Relat. Psychoses* 5, 193–200.
- Vojta, C., Kinosian, B., Glick, H., Altshuler, L., Bauer, M.S., 2001. Self-reported quality of life across mood states in bipolar disorder. *Compr. Psychiatry* 42, 190–195.
- Wagnild, G.M., 2009. The Resilience Scale user's guide for the U.S. The Resilience Center, Worden, MT English version of the Resilience Scale and the 14-item Resilience Scale (RS-14).
- Wagnild, G.M., Young, H.M., 1993. Development and psychometric evaluation of the Resilience Scale. *J. Nurs. Meas.* 1, 165–178.
- Wartelsteiner, F., Mizuno, Y., Frajo-Apor, B., Kemmler, G., Pardeller, S., Sondermann, C., Welte, A., Fleischhacker, W.W., Uchida, H., Hofer, A., 2016. Quality of life in stabilized patients with schizophrenia is mainly associated with resilience and self-esteem. *Acta Psychiatr. Scand.* 134, 360–367.
- Yalcin-Siedentopf, N., Hoertnagl, C.M., Biedermann, F., Baumgartner, S., Deisenhammer, E.A., Hausmann, A., Kaufmann, A., Kemmler, G., Muhlbacher, M., Rauch, A.S., Fleischhacker, W.W., Hofer, A., 2014. Facial affect recognition in symptomatically remitted patients with schizophrenia and bipolar disorder. *Schizophr. Res.* 152, 440–445.
- Yanos, P.T., Lucksted, A., Drapalski, A.L., Roe, D., Lysaker, P., 2015. Interventions targeting mental health self-stigma: a review and comparison. *Psychiatr. Rehab. J.* 38, 171–178.
- Yanos, P.T., Roe, D., Markus, K., Lysaker, P.H., 2008. Pathways between internalized stigma and outcomes related to recovery in schizophrenia spectrum disorders. *Psychiatr. Serv.* 59, 1437–1442.
- Yatham, L.N., Lecrubier, Y., Fieve, R.R., Davis, K.H., Harris, S.D., Krishnan, A.A., 2004. Quality of life in patients with bipolar I depression: data from 920 patients. *Bipolar Disord.* 6, 379–385.
- Yen, C.F., Cheng, C.P., Huang, C.F., Yen, J.Y., Ko, C.H., Chen, C.S., 2008. Quality of life and its association with insight, adverse effects of medication and use of atypical antipsychotics in patients with bipolar disorder and schizophrenia in remission. *Bipolar Disord.* 10, 617–624.
- Young, R.C., Biggs, J.T., Ziegler, V.E., Meyer, D.A., 1978. A rating scale for mania: reliability, validity and sensitivity. *Br. J. Psychiatry* 133, 429–435.