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Research report

Dimensions underlying outcome criteria in bipolar I disorder

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Abstract

Objective: Various subjective and objective criteria are used to assess outcome in bipolar disorder. In this study, we explored to what extent they reflect distinct categories and whether underlying dimensions can be identified.
Patients and methods: One-hundred and twenty-one subjects with at least three episodes of bipolar I disorder (DSM-IV) were assessed on average 4.8 years after hospitalization. We assessed 14 variables reflecting different outcome criteria including subjective quality of life (SQOL), self-rated and observer-rated psychopathology, and functioning and disability. A principal component analysis was computed across all outcome variables. Identified dimensions were correlated with sociodemographic characteristics, illness history, premorbid adjustment and personality traits.
Results: Three outcome dimensions were identified, i.e. a 'general subjective', a 'functioning/disability' and a 'manic/psychotic symptoms' dimension. Together they explain 69% of the total variance. The 'general subjective' dimension consists of SQOL scales and self-rated depressive symptoms. It is associated with comorbid anxiety disorders and personality disorders, high neuroticism and not having been in hospital in the last year. The 'functioning/disability' dimension comprises of criteria reflecting negative symptoms, disability and low functioning. It is associated with more prior illness episodes and low premorbid adjustment. The 'manic/psychotic symptoms' dimension consists of observer-rated manic and positive psychotic symptoms. It is correlated with not currently taking a specific medication.
Limitations: Cross-sectional design with a limited sample size.
Conclusion: The findings indicate that outcome criteria in bipolar I disorder can be grouped into three distinct dimensions reflecting (1) subjective appraisals, (2) functioning/disability and (3) manic/psychotic symptoms. While measurement of psychotic/manic symptoms has become a matter of course, until now few studies have assessed disability or subjective appraisal in bipolar illness. Therefore important aspects of bipolar illness might be overseen. For a better understanding, we suggest that longitudinal studies of bipolar I disorders should consider all three dimensions of outcome and measure them separately.
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Keywords: Bipolar disorder; Outcome assessment (health care); Quality of life; Disability evaluation

1. Introduction

Ever since Kraepelin's description of "manic-depressive insanity" (Kraepelin, 1899), the assessment of outcome has been of interest for bipolar illness, as the diagnosis is made longitudinally and the disorder has

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both episodic and persisting consequences. Various criteria are used as indicators of outcome including observer-rated assessment of acute psychopathology (manic and depressive as well as positive and negative psychotic symptoms), self-rated mood scales (including mood-charting), scales of functioning, interviews (and other observer-rated instruments) to measure disability and self-rated subjective quality of life (SQOL) scales. However, subjective (i.e. self-rated) evaluation criteria like SQOL have received relatively little attention in the research of bipolar affective disorders, while they have become an important topic in other areas of mental health research (Lauer, 1999), notably in schizophrenia and unipolar depression research.

How different outcome criteria in bipolar disorders correlate with each other, and to what extent they reflect distinct constructs, is still poorly understood. Yet, the overlap of different outcome criteria should be known to determine their relative specificity and importance.

We aimed to identify underlying dimensions for various subjective, i.e. self-rated, and objective, i.e. observer-rated, outcome criteria in a cohort of patients with chronic bipolar affective illness, focusing on the following questions:

(1) Can underlying dimensions of observer-rated and self-rated outcome criteria of bipolar illness be identified?
(2) How are such dimensions associated with illness specific factors, such as duration of illness, number of episodes, comorbidity, present treatment and premorbid adjustment, sociodemographic variables, such as age and gender, and personality traits?

2. Methods

2.1. Sample

This is a report from a follow-up study of inpatients with bipolar disorders of the Psychiatric University Hospital Halle (Germany) (Marneros et al., 2004). Two-hundred and seventy-six subjects with a history of bipolar affective disorder according to ICD-10 criteria (WHO, 1993) had been treated in the in the years 1993–2000. After a mean period of 4.8 years (range: 1.0–9.7 years, S.D. 2.5) we re-assessed 182 of them who were more than 17 years of age. At the time of the interview, patients were not hospitalized. As the natural long-term course of the illness was of interest, we did not set an upper age limit for the follow-up assessment. Subjects gave informed consent to take part in a multidimensional assessment of various psychiatric and psychological constructs. As we were interested in subjects with an episodic course, we limited the sample to subjects with at least three prior illness episodes ($n=151$). By excluding subjects with only one or two illness episode(s) we applied a "staging model" of bipolar illness (Berk, 2006; McGorry et al., 2006) to achieve higher sample homogeneity.

The original hospital diagnoses had been made with ICD-10. At re-assessment DSM-IV (APA, 1994) was applied. As a result, four subjects did not fulfill DSM-IV criteria for bipolar I disorder. To make the sample diagnostically homogenous, we limited this study to bipolar I patients according to DSM-IV ($n=147$). Five further subjects had to be excluded due to a relevant mental retardation or signs of organic brain disease. We only included subjects, who had complete data sets for all instruments, which finally limited the total number of subjects included into this study to 121.

2.2. Outcome criteria

Fourteen different outcome criteria were assessed. The self-rated Beck Depression Inventory (BDI, 21 items) (Beck et al., 1961) and the observer-rated Cornell Dysthymia Rating Scale (CDRS, 20 items) (Mason et al., 1993) were used to assess depressive symptoms. Manic symptoms were measured with the self-rated Mania Syndrome Score (MSS, 48 items) (Shugar et al., 1992) and the observer-rated Young Mania Rating Scale (YMRS, 11 items) (Young et al., 1978). Psychotic symptoms and general symptoms of psychopathology were documented with the observer-rated Positive and Negative Symptom Scale (PANSS) (Kay et al., 1987). It consists of three sub-scores: PANSS-P (7 items) for positive psychotic symptoms, PANSS-N (7 items) for negative psychotic symptoms and PANSS-G (16 items) to assess global psychopathology. Functioning was measured with the observer-rated one-item Social and Occupational Functioning Scale (SOFAS) (APA, 1994). For disability, we used the WHO Disability Assessment Schedule (WHO/DAS) (Jung et al., 1989; WHO, 1988), which is a semi-structured interview performed with the patient to elicit responses to a number of questions on several areas of functioning. The algorithm published by Wiersma et al. (2000) was used to compute disability scores in seven areas (partner relation, work, social withdrawal, household participation, general interest, self-care and social friction), from which we calculated a general disability index by summing up the seven single scores. SQOL was determined with the self-rated WHOQOL-BREF scale (26 items) (WHOQOL Group, 1998), which consists of five domains: physical health

(seven items), psychological (six items), social relationships (three items), environment (eight items) and general SQOL (two items) with a range from 0 (very poor SQOL) to 100 (maximum SQOL).

2.3. Other variables

Personality was measured on the German version of the NEO-FFI questionnaire (Borkenau and Ostendorf, 1994). Present state DSM-IV diagnoses were ascertained with the SCID-I and SCID-II interviews (Fydrich et al., 1997; Wittchen et al., 1997). We asked whether subjects had been hospitalized for their mental disorder in the past year and whether they were presently taking medication (lithium, anticonvulsants, antidepressant or antipsychotics), as this question can serve as an indicator for medication compliance.

Retrospectively, the prior course of illness was assessed. This was done with a methodology, which has been described elsewhere (Pillmann et al., 2002). As an episode, we defined a significant time (at least 1 week), during which a patient was either hospitalized or a severe disruption of daily duties appeared due to mental problems. As age at onset, we defined the age at the time of the first episode of a mental disorder which led to specific treatment or resulted in disruption of daily duties. Premorbid adjustment was assessed with the Premorbid Adjustment Scale (PAS) (Cannon-Spoor et al., 1982; Krauss et al., 2000)—an instrument, which evaluates the degree of achievement of developmental goals of a subject's life before the onset of the illness, as premorbid adjustment has been shown to be related to illness outcome (Carlson et al., 2002). In the German social welfare system, a relevant percentage of subjects with chronic mental illness receive disability payments due to their medical condition before they reach the age of regular retirement. This is related to illness outcome (Brieger et al., 2004a). We asked about subjects' status in this respect. Furthermore, we asked subjects about their monthly personal income (in €), which is also usually influenced by chronic illness.

2.4. Statistics

In a first step, we performed an exploratory principal component analysis with varimax rotation (extraction: eigenvalue >1.0) of all previously mentioned variables linked to outcome. Correlation of these dimensions were computed with clinical characteristics (number of prior episodes, comorbidity of personality disorders, of substance abuse and of anxiety disorders, hospitalization in the past year, present medication), sociodemographic variables (age, gender, income, disability payment), premorbid adjustment and personality (NEO-FFI) using two-sided Pearson r correlations for continuous variables and two-sided Spearman rho for dichotomous variables. Significance was set at $p<0.05$. Even in the light of the exploratory nature of this part of the study, we decided to apply a Bonferroni correction for multiple correlations to ensure the clinical relevance of the findings. Statistical analysis was done with SPSS V12.0.

3. Results

Sixty-six (55%) of the subjects ($N=121$) were men. Present state comorbidity (DSM-IV) occurred at the following rates: substance abuse disorders 33.9%, anxiety disorders 15.7% and personality disorders 22.3%. Eighty-seven (72%) of all subjects received disability payments.

Table 1
Outcome, clinical, sociodemographic and personality variables ($N=121$)

Variable	Mean	S.D.	Range
Outcome variables			
WHOQOL: physical health	63.4	17.0	14.3–100
WHOQOL: psychological	62.4	18.1	0–100
WHOQOL: social relations	61.2	20.5	8.3–100
WHOQOL: environment	68.5	13.1	31.3–100
WHOQOL: global	59.7	18.2	0–100
BDI: self-rated depression	10.0	9.5	0–58
CDRS: observer-rated depression	8.0	8.5	0–56
MSS: self-rated mania	4.7	6.3	0–29
YMRS: observer-rated mania	1.7	3.4	0–22
PANSS-P: observer-rated positive symptoms	7.9	2.5	7–26
PANSS-N: observer-rated negative symptoms	10.6	4.8	7–28
PANSS-G: observer-rated general symptoms	19.8	4.3	16–37
SOFAS: observer-rated functioning	71.0	12.3	40–95
WHO/DAS: observer-rated disability	7.2	6.4	0–29
Sociodemographic and clinical variables			
Age (years)	47.2	11.4	21–73
Duration of illness (years)	17.3	9.2	2.6–44
Number of prior episodes [a]	8.7	5.6	3–26
Monthly personal income (€) [b]	1172	747	51–4090
Premorbid adjustment: general adjustment	0.70	0.80	0–3.25
Personality (NEO-FFI)			
Neuroticism [b]	2.0	0.6	0.5–4.0
Extraversion [b]	1.9	0.5	0.8–3.0
Openness [b]	2.2	0.5	1.2–3.4
Agreeableness [b]	2.5	0.4	1.3–3.6
Conscientiousness [b]	2.6	0.5	0.8–3.8

[a] Three subjects with a long-standing rapid-cycling course are excluded, as episodes could not be counted reasonably.
[b] Data were missing for four subjects.

Twenty-nine subjects (24.0%) had been hospitalized in the past year for mental health problems, 14 subjects (11.6%) reported not currently taking lithium or any antipsychotic, antidepressant or anticonvulsant medication. Table 1 shows the results of the different outcome variables as well as further illness-related, sociodemographic and personality characteristics.

Principal component analysis of the self-rated and observer-rated variables linked to outcome led to a three component solution. The three dimensions can be seen as reflecting a 'general subjective', a 'functioning/disability' and a 'manic/psychotic symptoms' dimension of outcome. Together they explained 69.0% of the total variance. Table 2 shows the loadings.

The 'general subjective' dimension (component 1) consists of all five domains of SQOL and inverse scores of self-rated depression. The 'functioning/disability' dimension (component 2) is linked to a high level of negative symptoms and disability, and low functioning.

Table 2
Factor loadings: only loadings >0.35 are shown

Rating scale	Component 1 "general subjective"	Component 2 "functioning/ disability"	Component 3 "manic/ psychotic symptoms"
BDI: self-rated depression	**−0.82**		
WHOQOL: physical health	**0.78**		
WHOQOL: psychological	**0.86**		
WHOQOL: social relations	**0.74**		
WHOQOL: environment	**0.78**		
WHOQOL: global	**0.83**		
CDRS: observer-rated depression	−0.52	0.56	
PANSS-N: observer-rated negative symptoms		**0.87**	
SOFAS: observer-rated functioning		**−0.82**	
WHO/DAS: observer-rated disability		**0.83**	
PANSS-G: observer-rated general symptoms		**0.66**	0.40
YMRS: observer-rated mania			**0.89**
PANSS-P: observer-rated positive symptoms			**0.82**
MSS: self-rated mania			0.42
Eigenvalue	4.5	3.3	1.9
% of variance explained	32.2	23.3	13.5

Principal component analysis, varimax rotation.
Factor loadings >0.6 are printed in bold.

Table 3
Correlations between the three dimensions and clinical, sociodemographic and personality variables—only significant correlations are shown

Independent variable	Dimension 1 "general subjective"	Dimension 2 "disability"	Dimension 3 "manic/psychotic symptoms"
Monthly personal income (€) [a]		−0.34*	
Number of prior illness episodes [b]		0.33**	
Comorbid personality disorder [b]	−0.27*		
Comorbid anxiety disorder [b]	−0.30*		
Receiving disability payments [b]		0.51**	
Hospitalization in the past year [b]	−0.33**		
Not taking any medication [b]			0.24*
Premorbid general adjustment (PAS) [a]		0.61**	
Personality			
Neuroticism [a]	−0.65**		
Extraversion [a]	0.43**	−0.28*	
Openness [a]		−0.27*	
Agreeableness [a]			−0.29*
Conscientiousness [a]	0.41**	−0.35**	

*$p<0.05$, **$p<0.01$.
Age, gender and comorbid substance abuse showed no significant correlations. Probability was multiplied by 16 to correct for multiple comparisons (Bonferroni's inequality correction).
[a] Pearson r (two-sided).
[b] Spearman rho (two-sided).

The 'manic/psychotic symptoms' dimension (component 3) consists of scales measuring psychotic and manic symptoms. Two scales load on two components: Observer-rated depression is both inversely associated with the 'general subjective' and to the 'functioning/disability' dimension, while the general scale of the PANSS loads on both the 'functioning/disability' and 'manic/psychotic symptoms' component. The three components are orthogonal and do not correlate with each other.

The dimensions are correlated with several clinical, personality and sociodemographic variables (see Table 3). Low values of the general subjective dimension are positively correlated with the presence of a comorbid personality disorder or a comorbid anxiety disorder and a history of hospitalization in the past year. Furthermore, the general subjective dimension shows a strong negative correlation with neuroticism, while it has weaker positive correlations with extraversion and conscientiousness. The functioning/disability dimension is associated with the number of prior illness episodes, low premorbid adjustment, a low income and receiving

disability payments. Also, it is negatively correlated with extraversion, openness and conscientiousness. The manic/psychotic symptom dimension shows significant correlations only with not taking any illness specific (mood-stabilizing, antipsychotic or antidepressant) medication and low agreeableness.

4. Discussion

Fourteen variables used as indicators of outcome were collapsed into three independent dimensions, i.e. a general subjective, functioning/disability and psychotic/manic symptoms dimension. The three dimensional model explains 69% of the variance of all outcome variables used in this study.

The psychotic/manic symptom dimension has for a long time shaped the general perception of bipolar illness, where (psychotic) mania has been regarded as a core syndrome. This has been contradicted by prospective studies (Judd et al., 2003; Judd et al., 2002) showing that the symptomatic structure of bipolar affective disorder is primarily depressive rather than manic. Nevertheless, the psychotic/manic symptoms are central to the diagnosis the illness, as obviously there is no bipolar affective disorder without a hypomanic, manic or mixed affective episode. They lead to disruption of duties, to hospitalization and to behaviours, which may be regarded as socially problematic (low agreeableness)—and to reluctance to take medication, which according to recent treatment guidelines (American Psychiatric Association, 2002) would have been indicated for all subjects in this study.

The functioning/disability dimension represents the deleterious and at the same insidious effects of bipolar illness on role fulfillment, functioning and overall activity. It is predated by low premorbid adjustment and more prior illness episodes. It is associated with a lower household income and higher rates of disability payments. Observer-rated depression loads moderately on the disability dimension, as it is known that negative symptoms and depressive symptoms may overlap (Marneros et al., 1991). While many biological and psychological interventions aim to control the psychotic/mania dimension (and possibly the general subjective dimension), one may assume that they have only limited effect on disability.

Finally, the general subjective dimension is probably the one of greatest importance for patients themselves: It reflects the patient's perspective, i.e. the anxiety and depression they feel, and their personal appraisal of life circumstances. It consists of all domains of SQOL along with–inversely correlated–self-reported depressive symptoms. Comorbid personality disorders and anxiety disorders have a negative impact on this dimension. This dimension is strongly linked to neuroticism, with its underlying processes of emotional instability and negative cognition (Watson, 2000). It is also linked to not being hospitalised in the last year. It is somewhat unexpected that subjective evaluation criteria have been used rather infrequently in the evaluation of bipolar illness (Brieger et al., 2004b; Yatham et al., 2004). Nevertheless, they are of importance and relevance, in particular in the light of an emergent consumer orientation. One can assume that this 'general subjective' dimension resembles a 'general subjective appraisal factor' (Fakhoury et al., 2002; Priebe et al., 1998) which has been found to underlie various criteria of subjective evaluation in patients with schizophrenia and alcoholism. Akiskal et al. (2001) have shown that even in mania self-report is feasible and valuable, which is contrary to the idea that patients with mania are unreliable sources of information. In their study, the combination of clinician and self-observation produced a more precise phenomenology.

The abundance of rating scales and outcome instruments in psychiatric research has fostered a search for underlying dimensions. On the symptom level, factor analyses have been performed in various severe mental disorders including mania (Akiskal et al., 2003; Cassidy et al., 1998), schizophrenia (Lenzenweger, 1999; Smith et al., 1998) and disorders of a broad psychotic continuum (Toomey et al., 1998). In one longitudinal schizophrenia study, which used a three-factor model (positive symptoms, negative symptoms, disorganization) (Loffler and Hafner, 1999), only the negative symptom factor showed stability and prognostic relevance (for social disability and social development) over 5 years. In another study, which assessed outcome in schizophrenia in four domains (psychopathology, functioning, needs for care and SQOL), marked heterogeneity in outcome was reported depending on the domain considered (Ruggeri et al., 2001). Overall, in schizophrenia research, a disability factor seems established, which is strongly related to negative symptoms and is of greatest importance for prognosis (Wiersma et al., 2000), while other (symptom) factors lack temporal stability and have little or no prognostic relevance. In this respect, factors of subjective appraisal are understudied even in schizophrenia research, but clearly they are of great importance to better understand the patients' perspectives, their needs and their health behaviour (including service use). The dimensional model we describe here for bipolar disorders shows clear similarities to findings in samples with schizophrenia, and the three dimensional model of outcome might hold true across different disorders.

The main methodological shortcoming of this study is its cross-sectional approach. Thus, there is no information

on the temporal stability of the outcome dimensions. In the future, longitudinal studies should establish the stability of the factors over time and identify their sensitivity to change, with and without specific interventions. Also, the three-dimensional model needs to be replicated in other samples and other contexts using different assessment instruments. If it is consistent across samples, settings and instruments, a further step might be to develop new methods to assess each of the three dimensions more directly and efficiently. One step would be to look at the relation of the individual items that loaded on the factors, as they overlap to a large extent.

The findings suggest that there are three dimensions of outcome in bipolar I illness. A comprehensive outcome assessment would measure all three of them. As they reflect different and distinct aspects of outcome, they should be measured separately and specifically.

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