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ORIGINAL PAPER

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Bipolar I disorder with mood-incongruent psychotic symptoms

A comparative longitudinal study

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Abstract *Objectives* The purpose of this paper is to demonstrate similarities and differences between bipolar I patients with and without mood-incongruent symptoms (MIS) over a long period of time, independently of longitudinal syndromatic constellations. *Methods* The Halle bipolarity longitudinal study (HABILOS) prospectively investigates 182 patients meeting the DSM-IV criteria for bipolar I disorders over a long period of time ($\bar{x}$ = 16.84 years). One thousand five hundred thirty-nine (1,539) episodes have been evaluated with standardized instruments. Patients and episodes were divided into two groups (with and without MIS) and were compared on various levels. *Results* It was found: (1) The majority of the episodes of bipolar I patients during long-term course did not have MIS, but the majority of patients did. (2) Bipolar I patients with MIS differ from patients without MIS in the following features: (a) Bipolar I patients with MIS are more frequently males. (b) Bipolar I patients with MIS need treatment at a significantly younger age than those without MIS. (c) First manifestation of bipolar I disorder with MIS after the age of 50 is extremely seldom. (d) Bipolar I patients with MIS more frequently have relatives with schizophrenia. (e) Bipolar I patients with MIS more frequently become disabled and retire at a significantly younger age than patients without MIS and (f) Significantly fewer patients with MIS than those without MIS live in a stable partnership. *Conclusions* It can be concluded that bipolar I disorders with MIS are more severe disorders than bipolar I disorders without MIS. This finding in combination with the above results, however, can give rise to the conclusion that bipolar I disorders with MIS are the epiphenomenon of the overlap, possibly genetic, of a "schizophrenic spectrum" and a "bipolar spectrum" and their antagonistic influence creating a "schizo-affective" area between them as a kind of psychotic continuum between prototypes.

Key words bipolar I · mood-incongruent symptoms · overlap of the spectra · psychotic continuum · schizoaffective · antagonistic influence

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Introduction

Mood-incongruent psychotic symptoms were assumed by classical psychopathologists—such as Karl Jaspers [11] or Kurt Schneider [24]—as being "pathognomonic" for schizophrenia (if an organic or medical condition is excluded), especially the so-called "First Rank Symptoms" (FRS). The DSM-IV, however, has involved mood-incongruent psychotic symptoms in mood disorders as well. But accepting mood-incongruent symptoms (MIS) as belonging to mood disorders as well, the risk of confusing diagnostic entities, such as "pure" mood disorders with schizoaffective disorders and to some extent with schizophrenia and schizophreniform disorders as well increases. It is still necessary to find out the discriminating power of MIS, and the boundaries between pure mood disorders and the other psychotic disorders mentioned. Many studies have tried to find out the differentiating validity of MIS, both in the past [14, 17, 21, 22] and more recently [2, 3, 8–10, 12, 23, 25, 26].

The following contribution is one of the attempts mentioned above, including a long-term follow-up period. The study does not take into account the type of the index episode or manifestations of pure schizophrenic, schizophreniform or schizoaffective episodes during course, but only the fulfilled criteria for "mood bipolarity" according to DSM-IV. The main ideas of the present paper were

(a) to take the mood bipolarity as the common basis of the disorder, independently of the presence or not of MIS and also independently of its longitudinal syndromatic constellation (i.e., independently of whether single episodes fulfil the criteria only of mood, or additionally of schizoaffective, or even of schizophreniform episodes if mood bipolarity was present during course). It has been considered as *conditio sine qua non* that during course, the DSM-IV criteria for bipolar I mood disorder were fulfilled.
(b) to compare bipolar I patients with MIS during long-term course to bipolar I patients without MIS and to find out if there are relevant differences between the two groups trying to verify (or falsify) the hypothesis that bipolar I disorders with MIS form a special group of disorders, sharing some relevant features with schizophrenic or schizophreniform disorders.

Methods

The present paper is based on the Halle bipolarity longitudinal study (HABILOS) [18–20], which is a prospective and longitudinal clinical population study. All in-patients of the psychiatric department of the Martin Luther University, Halle–Wittenberg, Germany, who had been diagnosed as bipolar (affective and schizoaffective) between 1 January 1993 and 31 December 2000, were involved in the prospective follow-up investigations. The diagnosis "bipolar" was made according to DSM-IV and ICD-10 criteria. In this paper, we present DSM-IV diagnosed bipolar I patients ($N = 276$) showing the characteristics presented in Table 1.

By the end of the follow-up period, 30 patients had died. Of the remaining 246 patients, 49 (19.9%) refused further examination and 15 (6.1%) could not be examined, mainly because of a change of their place of residence. That means that a follow-up investigation was carried out in 74% of the living patients.

An *episode* has been defined as:

1. The manifestation of symptoms leading to in-patient treatment in a mental hospital.
2. The manifestation of symptoms leading to an out-patient treatment and additionally fulfilling the following criteria: (a) interruption of the usual activities of the patient (occupation, education or household activities), (b) repeated consultation of a psychiatrist or the family doctor/general practitioner because of a re-manifestation of symptoms or a worsening of already existing symptoms, (c) psychotropic medication in therapeutical doses.

Following the above-mentioned criteria, we evaluated 1,539 episodes manifested between first treatment and last point of the follow-up investigation ($\bar{x} = 16.84$ years.). One thousand one hundred thirty-three (1,133) episodes needed in-patient and 406 out-patient treatment. The disproportion between in-patient and out-patient treatment can be explained by some special features of the German health system, which supports—at least during the investigative period—the in-patient treatment. The instruments used throughout the whole study are given in Table 2 for information purposes, although some of them are not involved in this paper.

Table 1 The Halle bipolarity longitudinal study (HABILOS)

Total patients involved	$n = 276$
Follow-up investigated	$n = 182$
Gender distribution	
Males (%)	$n = 93$ (51.1)
Females (%)	$n = 89$ (48.9)
Age at first treatment (SD)	$\bar{x} = 31.13$ years (11.44)
Age at follow-up (SD)	$\bar{x} = 47.88$ years (12.62)
Duration of prospective follow-up (SD)	$\bar{x} = 4.83$ years (2.46)
Duration of the disorder (SD)	$\bar{x} = 16.84$ years (10.91)
Number of episodes	1,539
Number of episodes that needed an in-patient treatment	1,133
Number of episodes in out-patient treatment	406

Table 2 The instruments used

Depressive symptoms	Cornell dysthymia rating scale (CDRS)
	Beck depression inventory (BDI)
Manic symptoms	Young mania rating scale (YMRS)
	Mania self assessment scale (MSS)
Psychotic symptoms	Positive and negative syndrome scale (PANSS)
Level of functioning	Global assessment of functioning (GAF)
	Social and occupational assessment scale (SOFAS)
	Disability assessment scale (DAS-WHO)
Premorbid adjustment	Premorbid adjustment scale (PAS)
Socio-biographic inventory	Semi-structured interview (SOBI)
Quality of life	WHO-quality of life assessment—BREF
	WHO-QOL-BREF
Personality and temperament	NEO-five-factor inventory (NEO-FFI)
	Temperament evaluation of memphis, Pisa, Paris and San Diego auto-questionnaire (TEMS-A)
Diagnosis	Structured clinical interview for DSM-IV (SKID-I, SKID-II)

The study has been reviewed by the appropriate ethics committee and has therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki. All persons gave their informed consent prior to their inclusion in the study. Details that might disclose the identity of the subjects under study were omitted.

The data were gathered by two psychiatrists (S.R., A.T.) under the supervision of two senior psychiatrists (A.M. and P.B.). The statistical evaluation was carried out in the research department of the University Hospital by one of the authors (D.R.).

We are presenting some selected essentials, connected with the aims of this paper.

Results

Frequency

During the investigated course (mean duration = 16.84 years, SD = 10.91), although 66% of the patients developed MIS at least once (see Fig. 1), the great majority of episodes did not show any MIS: Out of 1,539 assessed episodes, 68% did not have any MIS, whereas 32% did. In the group of patients having MIS at least once ($n = 120$), a slight majority of the 1,003 assessed episodes (518 = 52%) did not have any MIS, but 485 (48%) did.

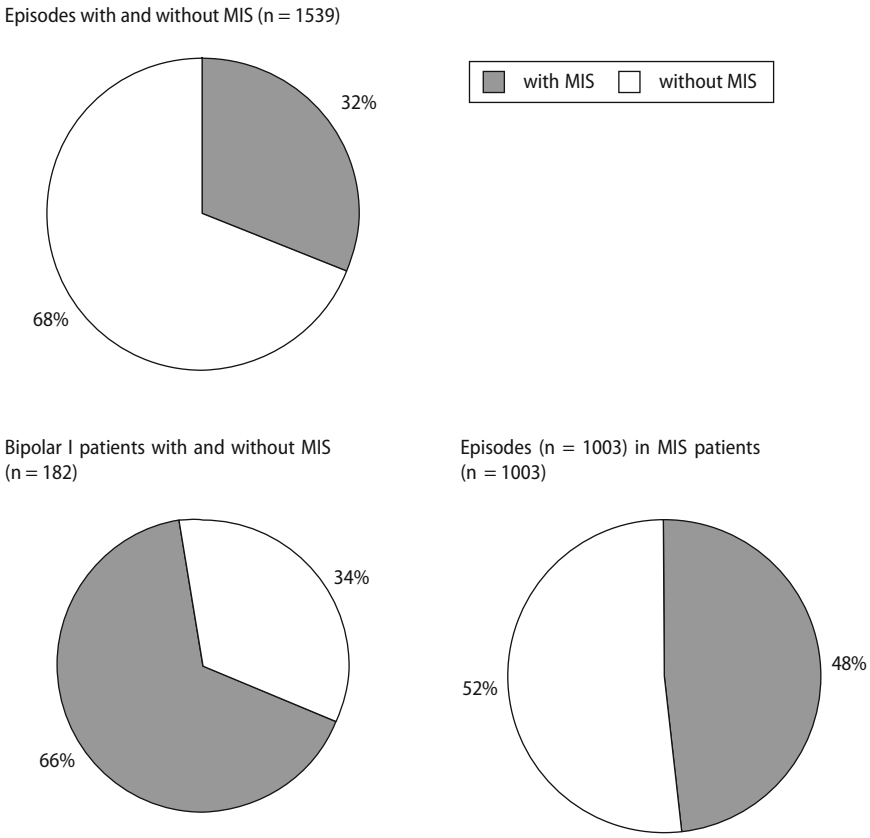

Fig. 1 Bipolar I disorder with and without mood-incongruent symptoms (MIS) during a period of 16.84 years

Sociobiographic data

Regarding *gender distribution*, 57% of all cases with MIS were found in males and 43% in females (Table 3). In contrast, bipolar patients not having MIS were most often females (60%).

Almost equal proportions of bipolar patients with and without MIS (57 vs. 56%) had at least one first- or second-grade *relative with a mental illness* (Table 3). Although in the group of bipolar disorders without MIS, the number of patients having relatives with mood disorders was found to be higher than in the group with MIS (44 vs. 36%), the statistic difference was not significant. The frequency of schizophrenic disorders among relatives of bipolar patients with MIS was significantly higher than in the group of pure bipolars (18 vs. 5%).

No significant difference between both groups was found regarding *season of birth, broken home situation* or *level of education*.

Table 3 Sociobiographic data

	Bipolars without MIS (n = 62)	Bipolars with MIS (n = 120)	P
Gender distribution: female (number, percentage)	37 (60%)	52 (43%)	0.037
Mental illness in the family (number, percentage)	35 (57%)	67 (56%)	NS
Mood disorder	27 (44%)	43 (36%)	NS
Schizophrenic disorder	3 (5%)	21 (18%)	0.017
Season of birth (number, percentage)			
Spring	15 (24%)	29 (24%)	NS
Summer	13 (21%)	28 (23%)	NS
Autumn	17 (27%)	23 (19%)	NS
Winter	17 (27%)	40 (33%)	NS
Broken home (number, percentage)	30 (48%)	45 (39%)	NS
Education level (number, percentage)			
Low	16 (26%)	28 (23%)	NS
Middle	28 (45%)	57 (48%)	NS
High	18 (29%)	35 (29%)	NS

χ^2 test

Table 4 Course of illness and outcome

	Bipolars without MIS (n = 62)	Bipolars with MIS (n = 120)	P
Age at first treatment (mean, SD)[a]	36.24 (12.48)	28.49 (9.94)	0.000
Duration of the disease (mean, SD)[b]	14.59 (10.09)	18.01 (11.18)	0.045
Number of episodes (mean, SD)[a]	6.13 (5.14)	8.30 (6.18)	0.016
History of suicide attempts (number, percent)[c]	32 (51.6%)	60 (50.0%)	NS
Disability pension (number, percent)[c]	30 (48.4%)	76 (63.3%)	0.053
Age at disability pension (mean, SD)[b]	44.97 (9.48)	37.08 (8.73)	0.000
Partnership[d]			0.001
No partnership	15 (24.2%)	54 (45.0%)	
Living together with a partner	44 (71.0%)	51 (42.5%)	
Relationship, but not living together	3 (4.8%)	15 (12.5%)	
Comorbidity (lifetime, number, percent)			
Alcohol/substances: dependence or abuse[c]	19 (30.7%) 10 (16.1%)	39 (32.5%) 14 (11.7%)	NS NS
Anxiety disorders[c]			
Level of functioning at follow-up			
GAF (mean, SD)[b]	75.8 (13.5)	72.5 (13.7)	NS
SOFAS (mean, SD)[b]	73.6 (14.4)	68.3 (14.2)	0.018
DAS-WHO (number, percent)[c]	23 (37.7%)	32 (27.1%)	NS
Good social adaption	22 (36.1%)	42 (35.6%)	
Satisfactory social adaption	11 (18.0%)	28 (23.7%)	
Moderate social adaption	4 (6.6%)	9 (7.6%)	
Poor social adaption	1 (1.6%)	7 (5.9%)	
Very poor social adaption			
Quality of life (WHOQOL-BREF, mean, SD)			
Physical[b]	61.3 (17.6)	64.6 (17.1)	NS
Psychological[b]	61.9 (19.0)	63.5 (17.3)	NS
Social relationships[b]	63.4 (20.1)	61.2 (20.3)	NS
Environmental[b]	68.6 (14.7)	69.1 (12.5)	NS

NS not significant, *SD* standard deviation
[a]Mann–Whitney *U* test
[b]*t* test
[c]$\chi 2$ test
[d]Number and percent, $\chi 2$ test

Course of illness and outcome

Bipolar patients with MIS needed treatment at a significantly younger age (mean 28.5 years) than bipolar patients without MIS (mean 36.2 years, see Table 4; Fig. 2) and had a slightly longer duration of the disease.

Considering different stages of age at first treatment, the most obvious difference (P = 0.005) was found in the age group between 21 and 25 years (Fig. 2). Of the patients with MIS, only one was first treated after the age of 55 years and none after the age of 60. Patients with MIS exhibited significantly more episodes during the course of illness (Table 4). Almost equal proportions of bipolar patients with MIS (50%) and without MIS (51.6%) attempted suicide at least once during the duration of the illness. At the end of the follow-up investigation, 48% of patients without MIS and 63% of those with MIS received a disability pension due to the mental illness (Table 4). Bipolar patients with MIS, however, received the disability pension at a significantly younger age than bipolar patients without MIS. Since age at disability pension was significantly related to age at first treat-

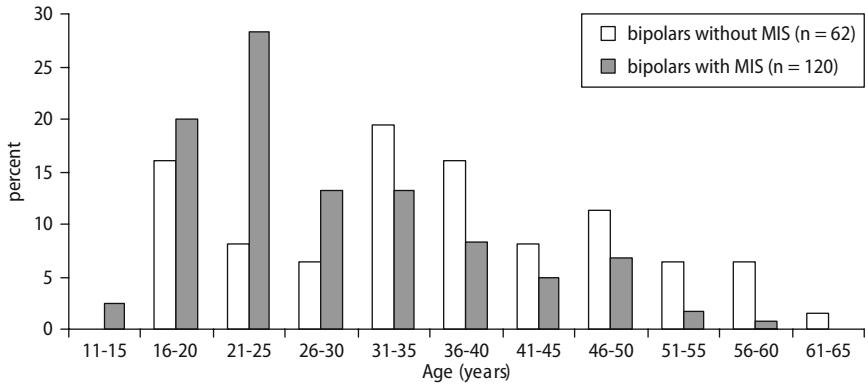

Fig. 2 Age at first treatment

ment ($r = 0.660$, $P = 0.000$), we included "age at first treatment" as covariate in the comparative analysis (ANCOVA). The difference between bipolar patients with and without MIS remained significant ($F = 4.437$, $P = 0.038$). Furthermore, both groups differed regarding to their mean SOFAS score ($P < 0.05$). However, there are no significant differences between both groups with respect to comorbidity (dependence, abuse, anxiety disorders), the quality of life scales or level of functioning examined by GAF or Disability Assessment Scale (DAS-WHO). Apart from the global rating of social adaptation we evaluated subscales (i.e., partner relationships, social withdrawal, work role, household participation, general interests) of the DAS-WHO. None of the subscales showed significant differences between bipolar patients with MIS and patients without MIS. However, with respect to the *work role* subscale there was a trend ($P = 0.066$) for more bipolars with MIS having at least some disability (72.7%) in comparison to bipolars without MIS (56.8%).

Conclusions and discussion

This study allows two main conclusions: first: whereas the majority of episodes of bipolar I patients during long-term course do not have MIS, the majority of patients do. Second: bipolar I patients with MIS differ from patients without MIS in some relevant domains having theoretical and clinical interest.

Investigating bipolar I patients longitudinally over a long period of time (over 16 years in the present study), and also investigating a great number of episodes (1,539 in the present study), it was found that—although most patients (66%) developed MIS at least once during long-term course (a finding which is conform with other studies [8])—the majority of episodes were pure mood episodes without any MIS (68% of the episodes).

The second relevant result of the present study is that bipolar I patients with MIS differ from patients without MIS in the following relevant domains of theoretical and clinical interest: (a) They are most often males. (b) They need treatment at a significantly younger age. (c) It is very rare that the disorder manifests for the first time after the age of 55. (d) Although the frequency of mental illnesses in their families is nearly the same as in the families of the patients without MIS (57 vs. 56%), the frequency of schizophrenia is higher than in the families of patients not having MIS (however, with a weak statistical significance). (e) Additionally, there are significant differences between the two groups regarding prognosis, especially disability and social consequences of the illness. One of the most robust indicators of disability and social consequences is the variable "disability pension" (as it excludes subjective estimations of the patients or subjective impressions of the investigator). Significantly more patients with MIS (63 vs. 48%) had to retire due to the mental disorder and also at a significantly younger age (approx. 37 vs. approx. 45 years of age) than patients without MIS and (f) significantly more bipolar I patients with MIS had no stable heterosexual (or in very few cases a homosexual) partnership than patients without MIS (45 vs. 24%). In spite of the fact that the mean age at investigation showed a statistically significant difference—albeit a weak one (50.72 vs. 46.4 years)—this finding perhaps only partially depends on the patients' age, because in both groups the youngest patient was 21 or 22 years old; that means all patients were at an age suitable for partnerships.

With regard to prognosis, the findings of the present study are consistent with those of some other recent studies, such as of Conus et al. [3], Dunayevich and Keck [8], Harrow et al. [9], and Strakowski et al. [25]. On the other hand, Keck et al. [12] in another study found no significant difference between bipolar patients with or without a history of psychosis in any demographic, psychosocial, vocational or course variables. However, the last mentioned study involved only out-patients who, in a substantial proportion, showed signs of a dysfunctional outcome already at the time of entry into the study. In a 15-year follow-up study Jager et al. [10] found that psychotic symptoms have only "prognostic significance with respect to re-hospitalisation, but not with respect to global functioning, symptom level, and social outcome 15 years after first hospitalisation". However, that study is limited to depressive patients and involved all psychotic symptoms, i.e., mood-congruent and MIS.

A finding which we did not anticipate was the fact that—although bipolar I patients with MIS became more frequently disabled and retired at a significant younger age than those without MIS—the difference between the two groups on the instrumental level showed only in SOFAS a tendency to statistical significance, but not in GAF or DAS-WHO global score. However, the trend for more bipolars with MIS having at least some disability with respect to the subscale *work role* (DAS-WHO) is in line with the difference between both groups with regard to frequency of disability pension. Nevertheless, the difference between the two groups regarding the SOFAS results demonstrates a relation between the instrumental findings and the social reality.

Also unexpected—given the differences regarding disability pension—is the non-existing statistical difference between the two groups regarding WHO-QOL. This finding might be explained by the disappearance of the occupational stress resulting from the confrontation with occupational demands and weaknesses and deficits due to the disorders. An isolated evaluation of items of the WHO-QOL concerning only occupational abilities is not intended. Another point, which might at least partially explain the phenomenon, is related to the German national retirement

system, providing a relatively efficient financial support for the disabled. This might compensate for some of the negative aspects of QOL.

Nevertheless, all the above-mentioned differences regarding gender, age at onset, family history and outcome support the assumption of some overlap of mood disorders with the schizophrenic spectrum, giving bipolar patients with MIS a position between prototypic schizophrenia and prototypic mood disorders [1, 7, 15, 16], perhaps due to genetics [4–6, 13].

The special characteristics of bipolar disorders with MIS can lead to similar conclusions as their polymorphism. As polymorphism we defined the phenomenon according to which also other episodes than mood episodes can occur during the long-term course of bipolar I disorders, e.g., schizophreniform and "schizo-affective" episodes (defined as concurrently fulfilling the criteria of both, schizophreniform and mood episodes) [17, 18]. It could theoretically be possible to argue that bipolar disorders with MIS (like polymorphic bipolar disorders) have at least two comorbid disorders: schizophrenia and bipolar disorder. We think that the construct of Comorbidity yet cannot explain the fact that patients with MIS (like bipolar patients with a polymorphic course) differ from patients with prototypic diseases, i.e., schizophrenia or mood bipolar disorders without MIS, on various relevant levels (age at onset, family history, outcome etc.). Perhaps the answer can be found in the "antagonistic influence" of both genetically determined or co-determined disorders the result of which is a position of mood disorders with MIS in-between the two prototypes [18].

However, there are some limitations: the study is not blind. The investigating psychiatrists were experienced, but they knew almost all patients. Therefore, it is impossible to exclude bias. The second partial limitation is the fact that the information about family history was retrieved from the patients and only partially from their relatives and therefore, may be incomplete. The fact that in this investigation the role of negative symptoms could not be evaluated for the whole period is another limiting factor, as well as the retirement due to the mental illness is strongly connected with specific national features.

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