SPECIAL ISSUE

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Affective and schizoaffective mixed states

■ **Abstract** Although both DSM-IV and ICD-10 define schizoaffective mixed states, they have not received much attention – neither in the clinical nor in research context. We present preliminary results of a prospective study of bipolar affective (n = 100) and bipolar schizoaffective (n = 177) patients. 25 % of the bipolar affective and 32 % of the bipolar schizoaffective patients had at least one (schizo)mixed episode during the illness course. Nevertheless, (schizo)mixed episodes were rare – only 5.6 % of all episodes. There was a trend that patients with (schizo)mixed episodes were more often women and exhibited more disability (reflected by higher rates of disability payments). Nevertheless, these differences failed to reach significance. Overall, schizo-mixed episodes are as frequent as "pure" affective mixed episodes. They might be linked to a less favourable course. Nevertheless, while their diagnostic criteria are problematic, they are systematically underdiagnosed.

■ **Key words** bipolar disorder · schizoaffective disorder · longitudinal studies

Introduction

The literature on mixed affective states is not very ample, but concerning schizoaffective mixed states there is practically no work available. This almost complete absence of scientific research on schizoaffective mixed states is a paradox and understandable at the same time [20, 23]. On the one hand, both ICD-10 [31] and DSM-IV [2] define a diagnosis "schizoaffective mixed episode", which is meant to enable clinicians and researchers to make the diagnosis "schizoaffective mixed episode" according to ICD-10 or DSM-IV criteria. On the other hand, the uncertainty of the definition of schizoaffective disorders in general [14], and the complexity of the clinical and psychopathological picture of schizoaffective mixed states in particular make diagnostic decisions difficult [30]. It requires substantial experience and training to make the diagnosis of schizoaffective mixed episodes correctly – possibly more than for diagnosing other psychotic or affective syndromes.

The ICD-10 [31] and DSM-IV [2] definitions of schizoaffective disorders and therefore also of their mixed episodes are insufficient, because they lack longitudinal perspectives [15, 20, 23]. In earlier papers we recommended an "empirical" definition of schizoaffective disorders [15, 18, 24, 25]. Unlike DSM-IV and ICD-10, we have defined schizoaffective disorders longitudinally dividing them into two types:

- *Concurrent type:* with at least one schizoaffective episode during the course. This means that both a relevant schizophrenic and an affective syndrome co-occur (i. e. schizodepressive, schizomanic, schizomanic-depressive mixed episodes, which to a certain extent overlap with the DSM-IV and ICD-10 concept of mood disorders with mood-incongruent psychotic features).
- *Sequential type:* the sequential manifestation of schizophrenic and affective episodes during the course, independently of the type and number of other episodes.

This definition was empirically validated [17, 18, 19, 21].

To answer questions concerning affective and schizoaffective mixed states, we carried out the "Halle Bipolarity Longitudinal Study" (HABILOS) [20, 23]. We will present some preliminary findings from that study.

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Methods

The Halle Bipolarity Longitudinal Study (HABILOS) included all patients with manic, schizomanic, and mixed (affective and schizoaffective) episodes, who had been treated in the Department of Psychiatry and Psychotherapy of the Martin-Luther University Halle-Wittenberg, Germany, during the years 1993 and 2000. Patients were re-assessed after a mean observation time of 5.1 years, when they were not in hospital treatment. Inclusion criterion was a history of bipolar affective disorder according to DSM-IV [2]. Exclusion criteria were 1) a relevant mental retardation revealed by an optional screening test for intelligence, the MWT-B [13], and 2) signs of organic brain disease (such as dementia), which was, when clinically indicated, controlled for with the Minimal Mental State Examination [7]. Characteristics of the study population are given in Table 1. Relevant instruments used in HABILOS are shown in Table 2.

Results

Altogether 277 patients fulfilled inclusion criteria as mentioned above. At the time of re-assessment 31 subjects (11.2 %) had died, in 9 of these cases we had information that subjects had committed suicide. 25 subjects (9 %) refused to participate in the re-assessment, 26 former patients (9.4 %) were untraceable – even with the help of communal registration offices. Thus overall we

Table 1 Study population

Total number of patients:	277
female:	135 (48.7 %)
Age of first illness episode (mean, range)	32.3 years (13.0–66.2)
Age at the end of the follow-up period (mean, range)	47.9 years (20.6–90.1)
Duration of the illness (mean, range)	15.7 years (1.2–58.3)
Prospective period (mean, range)	5.1 years (1.0–9.7)
Total number of episodes	2119

Table 2 Instruments at follow-up

Scope	Instrument
Axis I diagnosis DSM-IV	SKID-I [33]
Axis II diagnosis DSM-IV	SKID-II [8]
History of illness	Rating of episodes [18]
Medication	Documentation of medication
Depressive Symptoms	CDRS [26]
	BDI [3]
Manic Symptoms	YMRS [34]
Psychotic Symptoms	MSS [29]
Personality	PANSS [11]
Temperament	NEO-FFI [4]
Social Biography	TEMPS-A Questionnaire [1]
Premorbid Functioning	SOBI [18]
Social Disability	PAS [5]
Social Disability	DAS-M [10]
Global Functioning	SOFAS [2]
Quality of Life	GAS [6]
	WHOQOL-Bref [32]

were able to re-assess 195 subjects (70.4 %) of the original sample. Most of the preliminary data presented in this paper stem from the baseline assessment of the full sample.

■ Frequency of patients with mixed episodes

Using the above empirical longitudinal diagnosis of schizoaffective disorder, we allocated all patients of HABILOS into two categories: a) "bipolar affective patients", who during the entire course had only affective episodes (depressive, manic, mixed) but no schizoaffective or schizophrenic episodes; b) "bipolar schizoaffective patients", with schizoaffective episodes during course, or with schizophrenic and affective episodes, which occurred sequentially.

According to this definition 100 patients were diagnosed as "bipolar affective", and 177 as "bipolar schizoaffective". The relatively high frequency of bipolar schizoaffective diagnoses is certainly a result of the hospital's specialisation in schizoaffective disorders. Of the bipolar affective patients, 25 % had at least one ICD-10 mixed episode during course, while 32.2 % of the bipolar schizoaffective had at least one mixed episode (see Fig. 1). There was no statistically significant difference between the two groups.
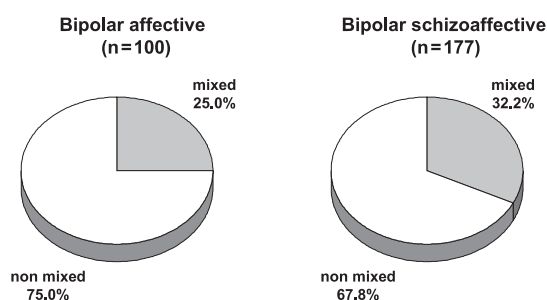
■ Types of episode

Although episodes were defined according to ICD-10, DSM-IV and Cincinnati Criteria [28], the findings presented in this paper regarding types of episode follow exclusively ICD-10 criteria. A total of 2119 episodes were documented. The most frequent type of episode was the depressive one (N = 613, 29 %) (see Fig. 2). Mixed episodes were found to be the rarest type of episodes: We found that 118 episodes (5.6 % of all episodes) fulfilled the ICD-10 criteria for mixed affective and schizoaffective episodes. Mixed affective episodes (n = 62; 2.9 %) were almost as frequent as mixed schizoaffective episodes (n = 56; 2.6 %).

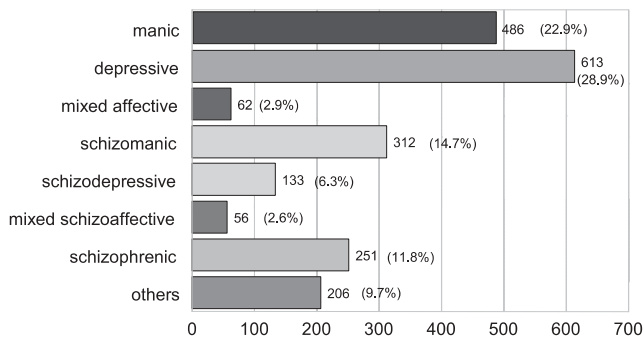**Fig. 1** Frequency of patients with at least one mixed episode during their illness course

Fig. 2 Types of episodes (2119 episodes in 277 patients)

Fig. 3 Length of hospitalisation

Length of episodes

As an estimate for "length of episode" we used "length of in-patient treatment". Obviously, this is not the real duration of an episode, but the two variables are highly correlated. Nevertheless, we found surprisingly few differences in the length of in-patient treatment between different episode types and the length of mixed affective episodes is surprisingly short.

Gender distribution

It is generally assumed that more women than men develop bipolar affective mixed states [27]. In our study, we found no significant differences between mixed and "non-mixed" patients concerning this gender distribution. On a (non-significant) descriptive level an over-representation of females in the group of mixed states was found in the group of pure affective mixed states, but not in that of schizoaffective mixed states, in which gender was almost equally represented. This is possibly a result of the impact of the schizophrenic syndrome. It is well known that in schizophrenia males are affected at similar rates as females, if not even over-represented [9]. As gender distribution in the whole bipolar group of
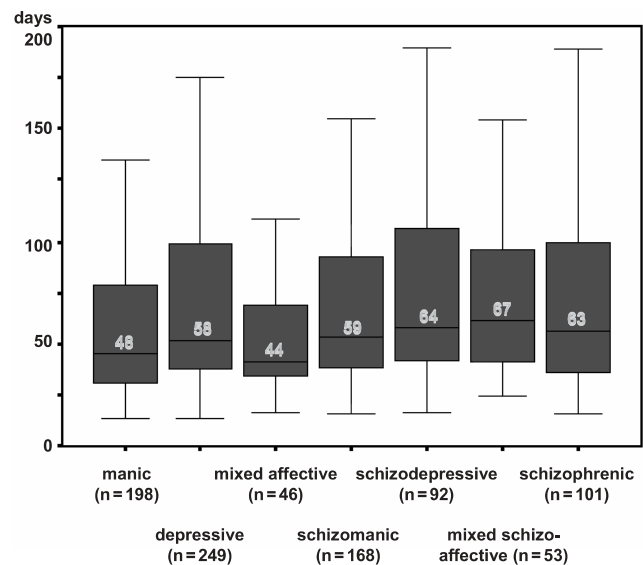
HABILOS is almost balanced, as it was expected, we can assume that findings regarding gender distribution in subgroups (like mixed states) are representative.

Type of first episode

In bipolar affective disorder the majority of first episodes were depressive, while in bipolar schizoaffective disorder first episodes were (schizo)depressive, (schizo)manic or schizophrenic at rather comparable rates. Interestingly, only 14 % of patients who developed a mixed bipolar schizoaffective course and 20 % of the patients with a mixed affective course had an initial mixed episode (Table 3).

As can be seen from Fig. 5, mixed episodes could occur at any time of the illness, which means, as bipolar affective disorders are chronic and highly recurrent [16], quite often a first mixed episode was observed even af-

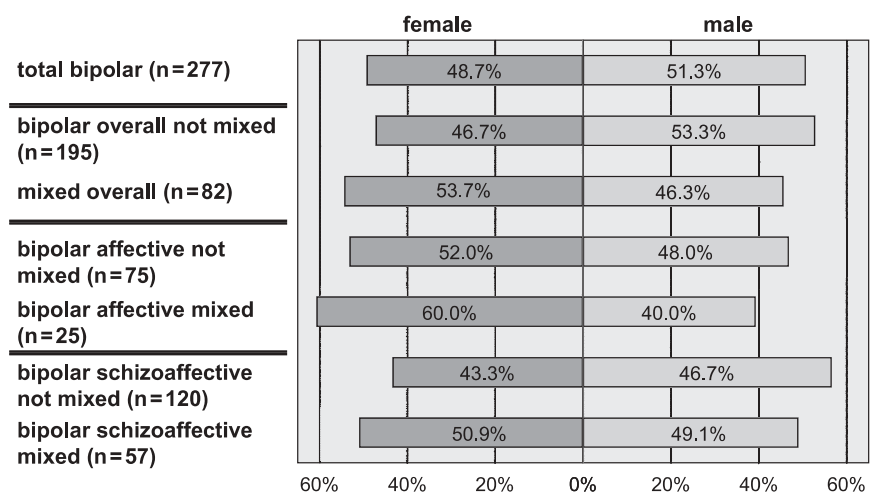**Fig. 4** Gender ratio (no significance)

Table 3 Type of first illness episode

	Bipolar affective disorders (n = 100)		Bipolar schizoaffective disorders (n = 177)	
	non mixed (n = 75)	mixed (n = 25)	non mixed (n = 120)	mixed (n = 57)
manic	28 (37.3 %)	6 (24.0 %)	13 (10.8 %)	2 (3.5 %)
depressive	45 (60.0 %)	13 (52.0 %)	25 (20.8 %)	21 (36.8 %)
mixed affective	–	5 (20.0 %)	–	–
schizomanic	–	–	29 (24.2 %)	6 (10.5 %)
schizodepressive	–	–	7 (5.8 %)	1 (1.8 %)
mixed schizoaffective	–	–	–	8 (14.0 %)
schizophrenic	–	–	41 (34.2 %)	13 (22.8 %)
not exactly classifiable	2 (2.7 %)	1 (4.0 %)	5 (4.2 %)	6 (10.5 %)
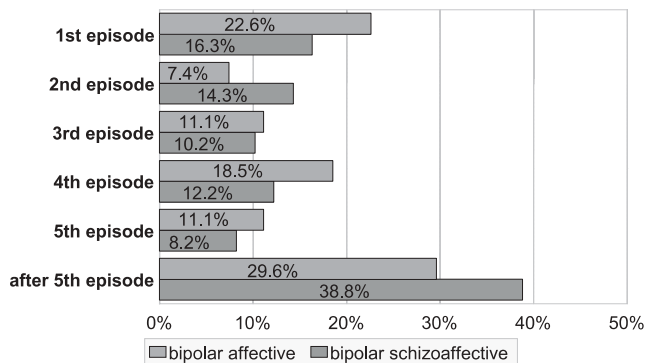
Fig. 5 First manifestation of mixed episode in the course of a bipolar illness

ter the 5th illness episode. This was already known to Kraepelin, who had pointed out that mixed states often appeared during later periods of the illness [12].

■ Disability pensions

In both the bipolar affective and bipolar schizoaffective patient groups, the proportion of patients receiving dis-

ability payment was higher in patients with mixed episodes (52 % versus 35 % in the affective group and 60 % versus 53 % in the schizoaffective group; Fig. 6). This may be seen as an indication that patients with mixed schizoaffective episodes have a worse prognosis, but again the observed differences missed significance.

Disability pension payments commenced at an earlier age in the group of schizoaffective patients (with a mean age of 36 years – see Fig. 7), which is very young compared to the average age for a disability pension (due to any cause) in the state of Saxony-Anhalt, which was 50.2 years in 1999.

Discussion and conclusions

The main two conclusions of these preliminary findings of HABILOS are the following:
- First, schizoaffective mixed states are as common as affective mixed states. But there is paucity of research on the topic (except for some earlier work of our group [18, 22]); at the same time they are underdiagnosed in spite of existing diagnostic criteria in ICD-10 and DSM-IV. The main reasons are the difficulty in
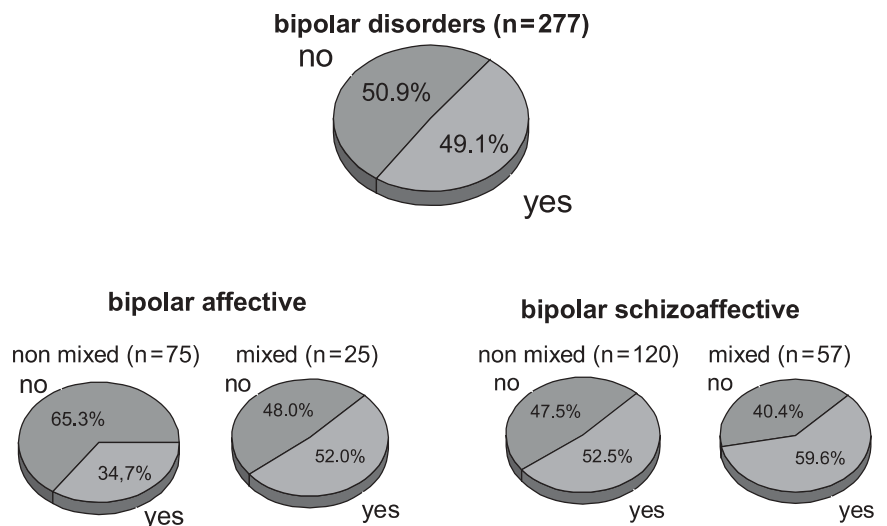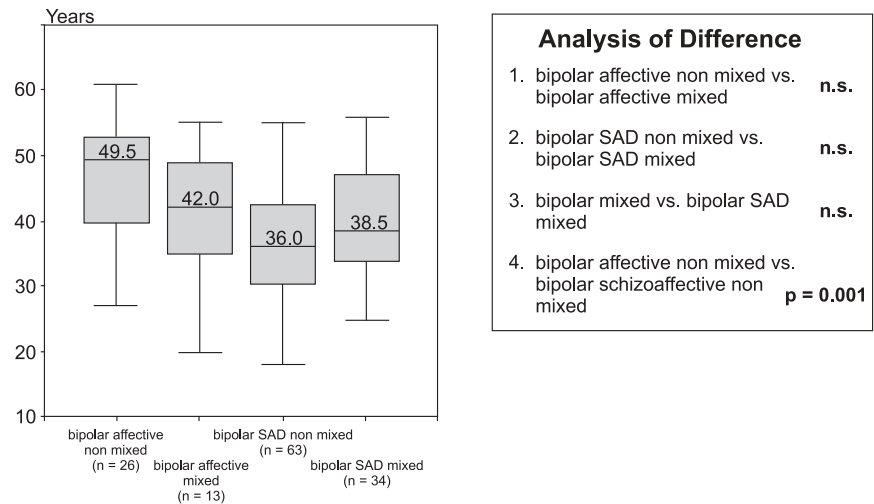
Fig. 6 Frequency of disability payments

Fig. 7 Age of first disability payment

Years

Analysis of Difference

1. bipolar affective non mixed vs. bipolar affective mixed — **n.s.**

2. bipolar SAD non mixed vs. bipolar SAD mixed — **n.s.**

3. bipolar mixed vs. bipolar SAD mixed — **n.s.**

4. bipolar affective non mixed vs. bipolar schizoaffective non mixed — **p = 0.001**

diagnosing "schizoaffective mixed state", the controversial concept of schizoaffective disorders, and the problematic diagnostic criteria. But because of their severity and prognostic value, schizoaffective mixed states can no longer be ignored.

- The second main conclusion of this paper is based on the knowledge that schizoaffective disorders occupy a position between affective and schizophrenic disorder regarding severity [18, 24, 25]. Schizoaffective disorders have a more unfavourable prognosis than affective disorders. There is some indication that schizoaffective mixed states are the most severe type within the bipolar spectrum: There may be a correlation with severe disability, which underlines its prognostic value.

Despite the fact that affective and schizoaffective mixed episodes are common in bipolar patients (approximately 40 % of all bipolar patients have at least one mixed episode during the course of their illness, [20]), they represent only a small proportion of all the episodes occurring during the course of the illness: Of 2119 episodes only 62 (2.9 %) were mixed affective and only 56 episodes (2.6 %) were schizoaffective mixed. The diagnostic stability of mixed episodes was obviously small. The majority of the episodes were depressive (28.9 %). In an earlier study we have had indication [18] that mixed affective episodes were longer than all other episodes occurring during the course of bipolar disorders. In this study, in contrast to our expectations and earlier findings, mixed affective episodes were relatively short – we observed no significant difference to other types of episodes concerning duration of hospital stay. One explanation might be the following: while in our former investigations many of the patients with mixed affective episodes received antidepressants and lithium and none of them anticonvulsants, in the HABILOS study almost all patients received anticonvulsants, while antidepressants were given very carefully. The potential shortening of episodes reflected by a shorter duration of hospital treatment may be a result of changes in treatment strategies.

Although many investigators have found that females are more frequently affected by mixed states, this finding is controversial (see [20, 27]). The present study found a trend towards an over-representation of females with mixed states only in the pure bipolar affective group, but not in the schizoaffective bipolar group. Chronicity of the illness certainly may have an effect on the manifestation of mixed episodes. A large proportion of patients with mixed states showed the first manifestation only after the third episode, although it appeared that "schizomixed" episodes could manifest themselves during any point of the illness. The prognosis of patients affected by mixed states may be less favourable, especially in the group of schizoaffective patients. Almost 60 % of schizoaffective patients with mixed states were receiving a disability pension at the time of the investigation – and this at very early age. Our study illustrates the necessity of more investigations on the topic of schizoaffective mixed states.

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