

Syndrome Shift in the Long-term Course of Schizoaffective Disorders*

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Summary. Seventy-two patients diagnosed as having schizoaffective disorders (Cologne study) were investigated with regard to syndrome shift. During long-term follow-up (mean 25.6 years) they had 400 episodes (the duration of an episode being defined as the time between the beginning and end of inpatient or inpatient-like treatment). A total of 61% of the patients had a *polymorphous* course, i.e. displayed more than one type of episode. The first syndrome shift was found in the early stages of the course (in 61% of the cases as early as the second episode, in 84% at latest by the third episode). Using diagnostic criteria considering the longitudinal approach, 88% of schizoaffective disorders could be definitively diagnosed as such at the latest by the second episode. The only difference in the course between polymorphous and monomorphous (with only one type of episode) schizoaffective disorders was that the former relapsed more frequently. On the basis of the findings of the present study we suggest a longitudinally based dichotomy of schizoaffective disorders into bipolar and unipolar.

Key words: Schizoaffective disorders – Course – Syndrome shift – Polymorphous – Monomorphous – Bipolar – Unipolar

Introduction

In a very informative article concerning the course of schizoaffective disorders Angst (1986), summarizing his own findings and those in the international litera-

ture, came to the conclusion that diagnostic shift in both directions, from affective to schizophrenic and vice versa, is frequently found in about 10% of patients over a longer period. Sheldrick et al. (1977), utilizing the findings of the International Pilot Study on Schizophrenia (WHO 1979), confirmed the observations of previous authors concerning syndrome shift from schizophrenic to affective episodes. Especially in schizoaffective disorders, some authors reported dramatic diagnostic changes (Cutting et al. 1978; Berg et al. 1983). The frequency of such changes, according to Angst, is a function partly of observation time, partly of diagnostic criteria (Angst 1986). Some authors speak of “misdiagnoses” in this respect (Horgan 1981; Mukherjee et al. 1983). The present study investigates the syndrome shift in the course of schizoaffective disorders.

Subjects, Methods and Definitions

Subjects

The present investigation is a part of the Cologne study on the long-term course and outcome of psychotic disorders (Marneros et al. 1986 a–c, 1988 a–c). It is based on the long-term observation of 72 patients with schizoaffective disorders. Material and subjects have been described elsewhere (Marneros et al. 1988a). We present here only the most important features (Table 1).

Definitions

The definitions and diagnostic criteria are described elsewhere (Marneros et al. 1986a, 1988a). Here we review only the most important points. The definitions applied distinguish between “episode” (defined cross-sectionally) and “disorder” or “illness” (defined longitudinally). The diagnostic criteria for episodes are based on the criteria and definitions of DSM-III (DSM-III-R), slightly modified. Eight different types of episodes are defined in this way: schizophrenic (SCH), melancholic (MEL), manic (MAN), manic-depressive mixed (MDE), schizodepressive (SDE), schizomanic (SMA), schizomanic-

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Table 1. Features of study population

Cologne study – schizoaffective disorders ($N = 72$)				
Sex	female	($N = 46$)	64%	ratio 1.8:1
	male	($N = 26$)	36%	
Age at onset (years)				M = 30.50 \bar{x} = 32.11 SD = 10.39 Min = 15.00 Max = 58.00
Age at end of follow-up period (years)				M = 57.50 \bar{x} = 57.72 SD = 13.58 Min = 27.00 Max = 87.00
Duration of follow-up period (years)				M = 25.00 \bar{x} = 25.61 SD = 10.46 Min = 10.00 Max = 59.00
Patients personally interviewed				100%
Place of interview				
– Patients visited us				39%
– Patients were visited at home				57%
– Psychiatric hospital/care unit				4%
Patients' relatives or relevant familiar persons interviewed additionally				56%

M = Median, \bar{x} = arithmetic mean, SD = standard deviation, Min = minimum value, Max = maximum value, N = number of patients

depressive mixed (SMD) and non-characteristic (UNC). For statistical purposes we consider an episode to last between the beginning and end of inpatient or inpatient-like treatment (intensive medical care and interruption of usual work or duties) (Marneros et al. 1988a).

Schizoaffective disorders are defined as the concurrent or sequential presence of schizophrenic (or mood-incongruent paranoid) symptoms and melancholic or manic symptoms.

The *affective symptomatology* has to fulfil the DSM-III (DSM-III-R) criteria of *melancholic type of major depression* or *manic episode*. It has been found that not every depressive or euphoric symptom qualifies a schizophrenic symptomatology as schizoaffective, but only melancholic or manic symptomatology (Marneros et al. 1986c, 1988d).

Methods

Methods and instruments of evaluation are described in detail elsewhere (Marneros et al. 1988 a–c). All patients were examined by the authors, and all case records were evaluated. The instruments of evaluation are shown in Table 2.

Data evaluation was carried out using the SPSSx computer system. Statistical methods have also been described by Marneros et al. (1988 a–c). Special tests will be referred to in the appropriate sections below.

Table 2

Cologne long-term study	
Instruments of follow-up investigation	
1. Present state examination (Wing/Cooper/Sartorius 1974)	
2. A modified version of PSE for follow-up investigations (Follow-up PSE)	
3. Course protocol consisting of:	
a) DAS	= Disability assessment schedule (Who 1978, 1986) ^a
b) FU-HSD	= Follow-up history and sociodemographic description schedule (WHO) ^b
c) DHSD	= Past history and sociodemographic description schedule (WHO) ^b
d) PIRS	= Psychological impairment rating schedule (WHO) ^a
e) GAS	= Global assessment scale (Spitzer et al. 1976)
f) Own completions, i.e. sociodemographic data, therapie etc.	
4. Case record evaluation	
Sections:	
a) Sociodemographic data	
b) Family history	
c) Broken home	
d) Life events	
e) History of illness	
f) Psychopathological symptoms (AMDP-oriented)	
g) Somatic findings	
h) Treatment	
i) Course and outcome of episode	

^aIn Schubart et al. (1986)

^bIn WHO 1979

Results

Frequency of Syndrome Shift

During a long-term course (mean 25.6 years), 61% of the patients showed at least one syndrome shift (*polymorphous*), while 39% did not (*monomorphous*).

Number and Type of Episodes Observed

During the observation time 400 episodes were registered. The great majority (83%) in the monomorphous group were schizodepressive episodes (Table 3). Although schizodepressive episodes were also the most frequent type in the polymorphous group, there they represented only 25% of the total, exactly the same as the schizomanic episodes.

Dividing the episodes into affective, schizophrenic, schizoaffective and non-characteristic or non-identifiable, we have the results shown in Table 3.

Table 3. Type of episode

Type of episode	Mono-morphous (N = 115)	Poly-morphous (N = 285)	Total (N = 400)
Schizoaffective	100%	64%	74%
– schizodepressive	83%	25%	42%
– schizomanic	4%	25%	19%
– schizomanic-depressive mixed	13%	13%	13%
Schizophrenic	–	10%	7%
Affective	–	20%	15%
– manic	–	4%	3%
– manic depressive	–	4%	3%
– melancholic	–	13%	9%
Non-characteristic/ Non-identifiable	–	6%	4%

Table 4. Initial syndrome

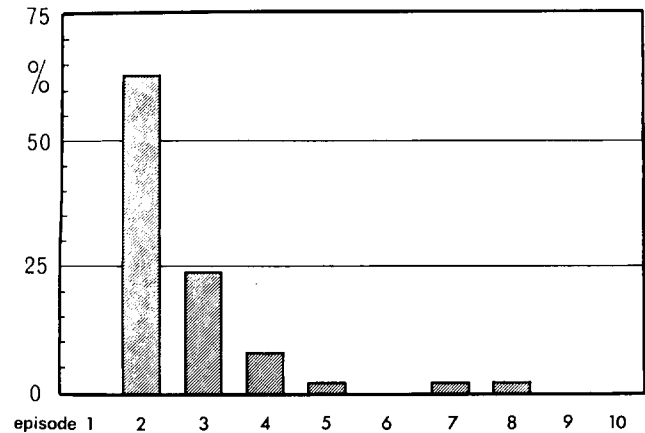
Type of episode	Mono-morphous (N = 28)	Poly-morphous (N = 44)	Total (N = 72)
Schizoaffective	100%	45%	67%
– schizodepressive	82%	30%	50%
– schizomanic	11%	11%	11%
– schizomanic-depressive mixed	7%	5%	6%
Schizophrenic	–	21%	13%
Affective	–	23%	14%
– manic	–	7%	4%
– manic depressive	–	11%	7%
– melancholic	–	5%	3%
Non-characteristic/ Non-identifiable	–	11%	7%

Initial Syndrome

The most frequent kind of first episode in the schizoaffective disorders was a schizodepressive episode. Table 4 demonstrates that approximately one-third of the schizoaffective disorders began with a schizophrenic or an affective episode, or even with a non-identifiable episode, and only later became schizoaffective.

When Did the Syndrome Shift Occur for the First Time?

In the majority of the polymorphous cases (61%) the syndrome shift began with the second episode, i.e. the second episode was not of the same type as the first (Fig. 1). In 23% of cases the shift occurred in the

**Fig. 1.** First syndrome shift in regard to number of episode (schizoaffective disorders, polymorphous type, N = 44)

third episode, in 9% in the fourth. In the remaining three patients the syndrome shift began in the fifth, seventh and eighth episode respectively. No further syndrome shifts were observed after the eighth episode.

The time after onset at which the syndrome shift occurred was dependent on the duration of the cycle (Marneros et al. 1988b). The number of years elapsing before the syndrome shift began was 4 (median) (mean 8.1, range 1–35) after onset.

When Could the Diagnosis of Schizoaffective Disorder be Definitively Established?

In two-thirds of cases the diagnosis of schizoaffective disorder could already be made in the first episode. In 88% of the patients the diagnosis could be established at the latest in the second episode, and in 96% of them at the latest in the third episode. Only in 4% (three patients) was the diagnosis established later than the third episode.

Although 33% of the patients had a non-schizoaffective initial episode, only three patients (4%) showed no schizoaffective episodes in their course. Thus only in these three patients was the diagnosis based solely on sequential schizophrenic and affective symptomatology.

From Which Episode to Which?

Schizoaffective Onset. Of the 36 patients with an initial schizodepressive episode, 13 showed a syndrome shift later.

Generally schizoaffective disorders with a schizodepressive first episode had a very stable course; of the 173 episodes recorded in such patients, 76% were schizodepressive ones (Fig. 2). The most frequent

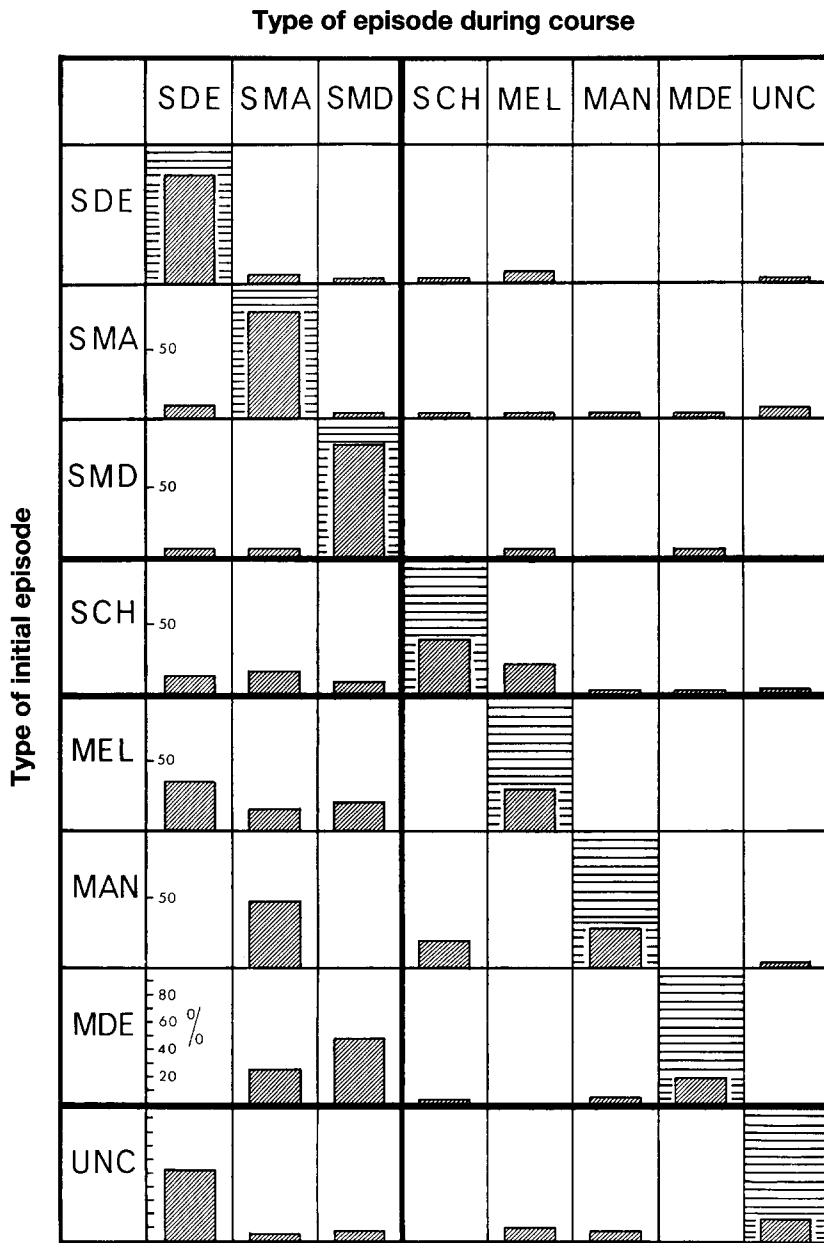


Fig. 2. Syndrome shift: frequency of the various types of episode depending on the type of initial episode

shift of patients with a schizodepressive first episode was into melancholic (MEL) and schizomanic (SMA) episodes: however, this occurred in only 8% and 6% of cases respectively.

Similar stability was shown by the schizoaffective disorders with schizomanic (SMA) and schizomanic-depressive mixed (SMD) first episodes; 77% and 81% respectively of the total number of episodes were of the same type as the initial episode (Fig. 2).

Fifty-four per cent of the patients had only schizoaffective episodes throughout (Table 5), while 46% of them also had schizophrenic or affective episodes.

Schizophrenic Onset. Only 38% of the total number of episodes of the patients with a schizophrenic first

episode were schizophrenic; 33% of them were schizoaffective, while 25% were pure affective (Fig. 2).

Affective Onset. Seventy per cent of the episodes of patients with a melancholic first episode were schizoaffective, while the remaining 30% were melancholic (Fig. 2). No schizophrenic, manic or manic-depressive mixed episodes were found among the 20 episodes of the patients with a melancholic first episode.

The most frequent type of episodes in patients with a manic first episode were schizomanic (47%). Interesting is the absence of depressive symptomatology in the course of these patients; no schizodepressive, melancholic, manic-depressive mixed or schizomanic-depressive mixed episodes were found.

Table 5

	Mono-morphous (N = 28)	Poly-morphous (N = 44)	Total (N = 72)
Only schizoaffective episodes	100%	25%	54%
With other types of episodes	–	75%	46%
– With schizophrenic episodes	–	39%	24%
– With affective episodes	–	57%	35%

Table 6. Sociodemographic data

		Mono-morphous	Poly-morphous	P
Sex	female	71%	59%	0.288 ^a
	male	29%	41%	
Sex ratio (m:f)		1:2.5	1:1.4	
Age at onset (years)		M = 30.5 \bar{x} = 33.5 SD = 11.2 Min = 18 Max = 58 N = 28	M = 30.5 \bar{x} = 31.2 SD = 9.9 Min = 15 Max = 50 N = 44	0.357 ^b
Duration of follow-up period (years)		M = 28.5 \bar{x} = 26.8 SD = 11.0 Min = 10 Max = 56 N = 28	M = 24.5 \bar{x} = 24.9 SD = 10.1 Min = 10 Max = 59 N = 44	0.451 ^b
Age at end of follow-up period (years)		M = 57.0 \bar{x} = 60.3 SD = 14.1 Min = 38 Max = 87 N = 28	M = 57.5 \bar{x} = 56.1 SD = 13.1 Min = 27 Max = 85 N = 44	0.197 ^b

^a χ -square test^b *t*-test

M = Median, \bar{x} = arithmetic mean, SD = standard deviation, Min = minimum value, Max = maximum value, N = number of patients

Almost half of all episodes of the cases with a manic-depressive first episode were schizomanic-depressive episodes; only 24% were pure affective episodes. No schizodepressive or melancholic episodes were found in this group; in contrast, all the episodes observed, with only one exception, had manic symptomatology according to our criteria.

Table 7. Features of course

		Mono-morphous	Poly-morphous	P
Average length of episode per patient (months)		M = 2.25 \bar{x} = 2.89 SD = 2.40 Min = 0.92 Max = 12 N = 27	M = 1.84 \bar{x} = 2.16 SD = 1.34 Min = 0.37 Max = 7.3 N = 44	0.046 ^a
Average length of intervals per patient (months)		M = 39.5 \bar{x} = 62.0 SD = 55.7 Min = 7.67 Max = 212.5 N = 19	M = 31.7 \bar{x} = 49.4 SD = 47.9 Min = 3.6 Max = 212.0 N = 44	0.350 ^a
Number of episodes		M = 3 \bar{x} = 4.18 SD = 3.87 Min = 1 Max = 16 N = 27	M = 6 \bar{x} = 6.45 SD = 4.02 Min = 2 Max = 18 N = 44	0.002 ^a
Annual frequency of episodes (AFE)		M = 0.12 \bar{x} = 0.17 SD = 0.15 Min = 0.03 Max = 0.74 N = 27	M = 0.25 \bar{x} = 0.31 SD = 0.25 Min = 0.08 Max = 1.42 N = 44	0.001 ^a
Average length of cycle per patient (months)		M = 43 \bar{x} = 66.8 SD = 58.2 Min = 9.6 Max = 227.8 N = 19	M = 35.4 \bar{x} = 52.6 SD = 49.4 Min = 8.2 Max = 226.0 N = 44	0.332 ^a
Number of cycles		M = 3 \bar{x} = 4.53 SD = 3.91 Min = 1 Max = 15 N = 19	M = 5 \bar{x} = 5.45 SD = 4.02 Min = 1 Max = 17 N = 44	0.323 ^a
Annual frequency of cycles (AFC)		M = 0.25 \bar{x} = 0.37 SD = 0.35 Min = 0.05 Max = 1.33 N = 19	M = 0.33 \bar{x} = 0.44 SD = 0.33 Min = 0.05 Max = 1.33 N = 44	0.330 ^a
Last relapse free period		M = 14 \bar{x} = 15.0 SD = 10.6 Min = 1.0 Max = 34.0 N = 27	M = 6 \bar{x} = 8.2 SD = 7.4 Min = 0 Max = 27.0 N = 44	0.007 ^b

^a *t*-test (log. values); ^b Mann-Whitney *U*-test

M = Median, \bar{x} = arithmetic mean, SD = standard deviation, Min = minimum value, Max = maximum value, N = number of patients

Table 8. Residuum

Residuum	Mono-morphous	Poly-morphous	P
Frequency	43%	55%	0.526 ^a
Years after onset	M = 1 \bar{x} = 3.9 SD = 7.1 Min = 0 Max = 25 N = 12	M = 4.5 \bar{x} = 6.4 SD = 6.7 Min = 0 Max = 22 N = 24	0.216 ^b
Number of episodes before residuum	M = 1 \bar{x} = 1.58 SD = 0.79 Min = 1 Max = 3 N = 12	M = 2 \bar{x} = 2.2 SD = 1.5 Min = 1 Max = 8 N = 24	0.249 ^b
Age at beginning of residuum	M = 39.5 \bar{x} = 38.1 SD = 10.3 Min = 24 Max = 54 N = 12	M = 34.5 \bar{x} = 37.2 SD = 10.7 Min = 19 Max = 68 N = 24	0.775 ^b

^a χ -square test; ^bMann-Whitney U-test

M = Median, \bar{x} = arithmetic mean, SD = standard deviation, Min = minimum value, Max = maximum value, N = number of patients

Non-characteristic Onset. More than half (54%) of the 39 episodes in the five patients with a non-characteristic first episode were schizodepressive episodes. All other types of episode were rare in this group (Fig. 2).

Comparison of Monomorphous and Polymorphous Schizoaffective Disorders

General Data. There were no significant differences between monomorphous and polymorphous schizoaffective disorders with regard to sex, age at onset, duration of the illness or age at the end of the follow-up period (Table 6).

Features of Course and Outcome. We compared the features of course and outcome of the two groups shown in Tables 7 and 8. For the comparison of the arithmetic mean we used the *t*-test, for the median the Mann-Whitney test.

There were significant differences between the two groups with regard to the number, annual frequency, and duration of episodes and the duration of the last relapse-free period. Polymorphous schizoaffective disorders had significantly more episodes, more frequent relapses, shorter episodes, and shorter

last relapse-free periods. There were no significant differences between the two groups with regard to duration of intervals and cycles. No differences in frequency and time of manifestation of residual symptoms were found (Table 8).

Conclusions and Discussion

Angst (1986) stated that one of the shortcomings of the concept of schizoaffective disorders consists in the restriction to a cross-sectional diagnosis, neglecting the natural history and the change of syndromes or "diagnoses" in subsequent episodes. The present study confirmed this statement, showing that the majority (61%) of the schizoaffective disorders displayed a syndrome shift, i.e. experienced more than one type of episode during the long-term course, including changes from one schizoaffective type to another, i.e. from schizodepressive to schizomanic and vice versa. Nevertheless, 46% had at least one pure affective or pure schizophrenic episode, while the other 54% had only schizoaffective episodes. The schizoaffective disorders can be divided, according to the findings of the present study, into a *polymorphous* group, i.e. those with more than one type of episode, and a *monomorphous* group, with only one type of episode. This conclusion is in agreement with some earlier investigations (Angst 1980, 1986; Angst et al. 1978, 1979; Berg et al. 1983; Brockington et al. 1980a, b; Kendell 1986; Maj 1985; Rzewuska and Angst 1982; Winokur et al. 1985).

Although it seems logical that the duration of the illness could have some influence on the type of course – the longer the course, the greater the chance of a syndrome shift – this assumption has not been confirmed by the present study. We think that two factors could explain this:

1. The shortest course in the Cologne study was 10 years, which is really a long time considering that the first syndrome shift occurred earlier (median 4 years after onset).
2. The syndrome shift correlates significantly with the number of episodes, and so only indirectly with the time since onset of the illness (in 84% of the patients the first syndrome shift occurred at latest in the third episode).

No differences other than those regarding symptomatology and course features were found between monomorphous and polymorphous schizoaffective disorders; for instance, there were no differences regarding sex, age at onset, family history of mental illness or personality type other than "sthenic". The finding that the sthenic/high-self-confident personal-

ity type was significantly more frequent in the polymorphous group could be explained by the fact that a significantly high proportion of polymorphous schizoaffective disorders are bipolar, a feature associated significantly with this personality type (Marneros et al., in preparation).

By defining schizoaffective disorders not only cross-sectionally but also longitudinally, it becomes obvious that some schizoaffective disorders begin with schizophrenic or affective symptomatology. This was the case in one-third of the present population, whose first episode was pure schizophrenic, pure affective or, sometimes, non-characteristic. This gives rise to the question: When can the diagnosis of schizoaffective disorder be definitively established? The present study gives a clear answer: relatively soon! *In 88% of the patients the diagnosis could be definitively established at latest in the second episode, and in 96% at latest in the third episode.* Any answer to the above question in regard to chronology has to consider the various factors influencing the length of the cycles (Angst 1980, 1986; Angst et al. 1978; Marneros et al. 1988b).

As the polymorphous course involves pure schizophrenic and pure affective episodes (10% and 20% respectively of the total number of episodes) we have to ask: Are such disorders really schizoaffective? The comparative study did not support a separation of the schizoaffective disorders with pure schizophrenic or pure affective episodes from those without such episodes.

Another interesting finding of the present study concerns the sequential symptomatology. Although one-third of the 72 patients had a non-schizoaffective initial episode, only 3 patients had still had only sequential symptomatology by the end of the observation time. Thus 96% had at least one episode featuring both schizophrenic and affective symptomatology. This finding supports to some extent the validity of definitions of schizoaffective disorders involving sequential symptomatology (Maj 1985; Angst 1986; Marneros et al. 1986a, 1988a, d).

The majority of the episodes (74%) were schizoaffective, that is a higher figure than that found by Rzewuska and Angst (1982) (55%) and by Angst et al. (1979) (51%).

Polymorphism does not necessarily involve great phenomenological instability. The present investigation suggests, in fact, good *phenomenological stability*, especially if the initial symptomatology is schizoaffective. If the first episode of the disorder is a schizoaffective one the great majority of the total number of episodes (76%–81%) will be of the same type. We thought that this phenomenological stability might suggest some kind of independence for the

schizoaffective disorders beginning with schizoaffective symptomatology. However, the comparison of the premorbid, sociodemographic and course features of that group with those of the group of schizoaffective disorders with a schizophrenic or affective onset did not support this assumption.

An interesting kind of phenomenological stability was shown by the schizoaffective disorders with a pure affective onset. In agreement with the findings of others (Coryell and Winokur 1980; Winokur 1974) these disorders usually change from affective to schizoaffective symptomatology and vice versa, but only very seldom (4 of 75 episodes) to pure schizophrenic symptomatology.

The greatest phenomenological instability was found in the cases with initially pure schizophrenic symptomatology, which showed almost equal frequencies of schizophrenic, affective and schizoaffective episodes overall.

A polymorphous course correlated significantly, as had been expected, with a bipolar type (68% of the polymorph group were bipolar), monomorphous course to the unipolar type (82%) (Marneros et al., in preparation).

The results of this investigation support the opinion that the dichotomy schizodepression/schizomania has only limited reliability and is only useful cross-sectionally (Brockington et al. 1980a, b; Kendell 1986). This is due to the polymorphism of schizoaffective psychoses; a division between schizodepression and schizomania is not always sufficient to characterize a schizoaffective disorder longitudinally. Therefore the reliability of comparisons of findings concerning, for instance, sociodemographic data, course, outcome or prophylaxis, based on the above dichotomy, is limited.

We suggest, considering the findings of the present investigation, avoiding the dichotomy between schizodepression and schizomania, which is only useful cross-sectionally, and using instead, in a similar way, the terms bipolar and unipolar, as in pure affective disorders (Angst and Scharfetter 1988; Marneros et al., in preparation).

Putting this into practice, we achieve the following: (a) inclusion of the longitudinal aspect and thus consideration of the syndrome shift; (b) inclusion of pure affective and pure schizophrenic syndromes manifesting during the course of the schizoaffective disorders; (c) more reliable comparison with pure affective disorders; (d) more precise definitions of subgroups of schizoaffective disorders, useful for genetic, biological and follow-up investigations.

Finally, the fact that there is a frequent syndrome shift in schizoaffective disorders might support, to some extent, the assumption of a psychotic continuum

between the two poles affective (unipolar) and schizophrenic (Crow 1986).

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