Eur Arch Psychiatr Neurol Sci (1988) 237:276–282

European Archives of Psychiatry and Neurological Sciences

Long-term Course of Schizoaffective Disorders*

Part II: Length of Cycles, Episodes, and Intervals

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Summary. Length of cycles, intervals, and episodes of 72 schizoaffective patients were investigated (duration of the follow-up $\bar{x} = 25.6$ years, minimum 10, maximum 59 years). The average cycle length (time between beginning of an episode and next relapse) was found to be 37.5 months (median). Patients with a schizodepressive initial episode, unipolar course, and without precipitating factors relapsed much later than patients with schizomanic onset, bipolar course, and precipitating factors. The older the patient at onset the shorter the first cycle. The length of cycle decreased with increasing cycle number. Patients with schizodepressive onset, asthenic personality, and monomorphous course stayed in hospital longer or needed longer inpatient-like treatment than others. Length of cycles and intervals were characterized by an extraordinary intraindividual and interindividual variation.

Key words: Schizoaffective disorders – Long-term course – Cycles – Intervals

1. Introduction

The length of cycles and of their component elements (episodes and intervals) is one of the most important variables in the course of schizoaffective disorders. As shown in Part I of the present study (Marneros et al. 1988a), schizoaffective disorders are recurrent. The aim of this part of the study was to establish when manifestations of new episodes occur, how long the intervals between episodes are, and which factors have an impact on them. The part of the Cologne study presented here is oriented strongly on the investigations carried out by Angst and co-workers (1973, 1988), because of the latter's fundamental importance, but also because of the dearth of other similar investigations in the international literature (Marneros and Tsuang 1986; Tsuang and Marneros 1986).

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*Supported by the German Research Association (Deutsche Forschungsgemeinschaft) by grants No. Ma 915–1/1 and Ma 915–1/2. The data analysis and statistical evaluation were carried out in the Institute for Medical Documentation and Statistics of the University of Bonn (Head: Prof. Dr. M. P. Baur)

2. Materials and Methods

Features of the investigated patients, methods, instruments, and definitions are described in Parts I and III (Marneros et al. 1988a, b). The necessity for various statistical procedures (logarithmic transformation, correlation analysis, stepwise multiple regression analysis, or special statistical considerations) will be described in the various subsections of the *Results* section.

3. Results

3.1 Cycles

3.1.1 Length of Cycles. A cycle was defined (Angst 1986) as the period of time between the beginning of one episode and the beginning of the next. As shown in the first part of this study, the 71 patients (1 permanently hospitalized patient excluded) passed through up to 17 cycles during the whole course, giving a total of 326 cycles. The average length of cycles 1 to 10 is shown in Fig. 1. However, more than 10 cycles were found in only a few cases, so that statistical conclusions with general validity were difficult;

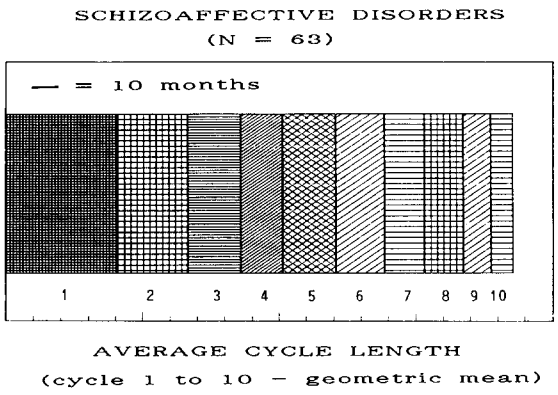

Fig. 1

Table 1. Length of cycles (months). Schizoaffective disorders ($N = 63$)

Cycle no.	N (patients)	Arithmetic mean	LN $\bar{x}$	Geometric mean	Median
1	63	79.67	3.70	40.49	32.00
2	57	46.84	3.24	25.76	32.25
3	40	29.98	2.97	19.57	16.75
4	34	21.91	2.73	15.41	14.00
5	30	25.49	2.96	19.32	16.75
6	26	29.78	2.88	17.85	14.00
7	17	20.72	2.68	14.72	12.50
8	11	21.59	2.64	14.07	14.00
9	10	19.55	2.32	10.26	8.87
10	10	11.32	2.07	8.00	11.00
11	8	13.21	2.25	9.57	13.75
12	6	11.83	2.34	10.47	12.50
13	5	20.80	2.49	12.11	8.00
14	3	30.41	3.05	21.26	33.50
15	3	19.50	2.20	9.09	6.00
16	2	21.87	2.76	15.80	21.87
17	1	21.00	3.04	21.00	21.00

the features of cycles 10 to 17 in these cases could not be considered as much more than features of the course of individual patients. The cases showed how variable is the course of schizoaffective disorders regarding length of cycles. Because of this individual variation it was important which value was taken as representative for the average length of cycles: the arithmetic mean gave the impression of a much more favorable course than the median or the geometric mean (Table 1).

Other authors (Angst and Weis 1967; Angst et al. 1973; Angst 1980) found that the length of cycles, intervals, and episodes can be transformed logarithmically to be normally distributed. This finding was checked and found to be valid for our material. The distribution of the lengths of cycles was found to be very strongly left-biased, i.e., the arithmetic mean presented the false picture of a very favorable prognosis regarding relapse, which was not the case for the median and geometric mean. Using logarithmic transformation an approximately normal distribution was achieved. Therefore, for the statistical investigations and conclusions regarding length of cycles, intervals, and episodes the logarithmically transformed values were used.

Table 2. Length of cycles 1 to 4 in patients having at least 4 cycles ($N = 34$) (months). Schizoaffective disorders

Cycle	LN $\bar{x}$	Geometric mean	Median	Paired t-test
1	3.67	39.65	32.37	
2	2.93	18.91	16.87	$P = 0.005$
3	3.01	20.49	17.87	$P = 0.694$
4	2.73	15.33	14.00	$P = 0.120$

Aiming to achieve data for generalization, we decided to include in the following statistical evaluation only as many cycles as were found in at least half the patients. At least four cycles were found in 34 patients (54% of the 63 patients having cycles). The length of these four cycles is shown in Table 2. Comparison of the successive cycles showed that a significant difference existed between the first and the second cycle ($P = 0.005$, log values, paired t-test) and also between the first and the third ($P = 0.004$) and fourth ($P = 0.000$) cycles, but not between the other successive cycles. The fourth cycle was found to be less than half as long as the first one.

However, there were very strong intraindividual and interindividual differences. Only two patients displayed a successive decrease in the length of the first four cycles, and in both of them the fifth cycle was longer than the fourth. Table 3 and Fig. 2 demonstrate the deviation, showing the frequency of successive increases or decreases in cycle length.

3.1.2 Average Length of Cycles. Aiming to achieve a more representative average cycle length, the intraindividual mean was computed, and then these values were used to calculate the average cycle length for the whole group (median). As already shown by other investigations (Angst 1980), this value is more representative than the mean of all cycles together. For statistical analysis the values were logarithmically transformed, using 63 patients, i.e., the whole investigated population minus 8 monophasic patients and 1 permanently hospitalized patient. The average cycle length was found to be 37.5 months (median, Table 4), i.e., the average time between the begin-

Table 3. Individual analysis of length of cycles in patients having at least 4 cycles ($N = 34$). Schizoaffective disorders

	Number patients
1) Every successive cycle shorter	2
2) Every successive cycle longer	0
3) Length of 2 cycles increasing, of 1 cycle decreasing	15
4) Length of 2 cycles decreasing, of 1 cycle increasing	15
5) Length of 2 cycles decreasing, 1 cycle unchanged	1
6) One decreasing, 1 increasing, 1 cycle unchanged	1
	34

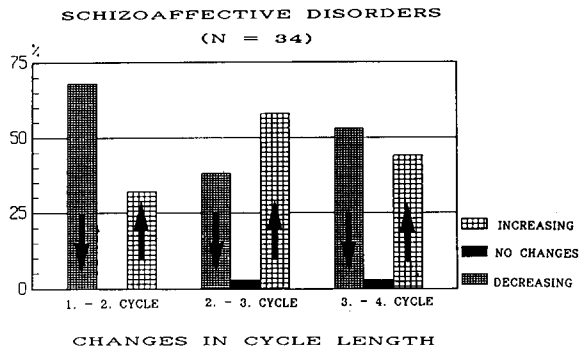

Fig. 2

Table 4. Average length of cycles (months) (intraindividual mean values). Schizoaffective disorders

Median	37.50
$\bar{x}$	56.87
Min.	8.25
Max.	227.75
LN $\bar{x}$	3.34
Geometric mean	28.22
Number of patients	63

ning of one episode and the beginning of the next one was over 3 years. Using the median of all cycles together ($N = 326$), instead of the median of the intraindividual mean values, the average cycle length was 17 months (Angst 1980, found almost the same, namely 18 months). This value falsely implied a very unfavorable course with regard to time of relapse.

3.1.3 Factors Influencing Average Cycle Length. Using univariate statistical analysis of the logarithmically transformed values (t-test) and Pearson correlation analysis, the influence of different factors shown in Tables 5 and 6 on the average cycle length was investigated. Polarity was the only factor to have an influence: patients with a bipolar course had on average significantly shorter cycles than unipolars.

The Pearson correlation analysis (Table 6) showed that none of the parameters investigated correlated significantly with the average length of the cycles (log). Nevertheless, findings of other authors showing a strong dependence of cycle length on age at onset (Angst 1980, 1986), were partially confirmed. The average cycle length was found to be independent of age at onset, but the first cycle (albeit not the others) was strongly dependent on this factor ($r = -0.4033$, $P = 0.001$), the older the patient at onset, the shorter the first cycle (see Sect. 3.1.4).

3.1.4 Length of First Cycle. The length of the first cycle differed significantly from that of the successive ones. The same factors investigated for average cycle length (Tables 5 and 6) were investigated for the length of the first cycle in all 63 patients with more than one episode. Using the t-test, patients with a schizodepressive first episode had a longer first cycle than patients with a schizomanic one. Patients with unipolar course and patients without precipitating factors also had longer first cycles. In addition, Pearson correlation analysis showed that the first cycle (log) was strongly (negatively) dependent on age at onset ($r = -4033$, $P = 0.001$): the older the patient at onset, the shorter the first cycle (Sect. 3.1.3). The average length of the first cycle in the investigated population was 32 months (median, range 1–372 months).

Stepwise multiple regression analysis including all univariate significant variables showed (Table 7) that the variables of age at onset, precipitating factors, and schizodepressive initial episode were selected by the stepwise procedure, explaining 35% of the variance.

3.2 Length of Episodes

The length of an episode (demarcated by the beginning and the ending of actual clinical symptomatology) can seldom be precisely defined. For this reason we decided for the purposes of statistical analysis to consider episode length in terms of the time between beginning and ending of inpatient or inpatient-like treatment (inpatient-like treatment meant (a) need for intensive medical care, i.e., treatment with psychotropic drugs and frequent consultations with a psychiatrist, and (b) interruption of usual occupation or duties). The mean intraindividual length of episodes of the 71 patients (1 permanently hospitalized

Table 5. Average length of cycles. Schizoaffective disorders ($N = 63$)

Variables	Total	N	Geometric mean	Median	P-values	
Sex	63				0.530	(1)
Female		40	29.72	42.5		
Male		23	25.77	22.2		
Personality	60				0.587	(2)
Obsessoid		15	31.71	56.0		
Sthenic/high-self-confident		19	23.84	25.5		
Asthenic/low-self-confident		26	29.50	35.4		
Premorbid social interactions	63				0.055	(1)
Tendency to social isolation		13	42.27	82.1		
No tendency to social isolation		50	25.39	35.4		
Broken home situation	63				0.340	(1)
Broken home		22	32.50	53.2		
No borken home		41	26.15	34.4		
Stable heterosexual relationship before onset	63				0.195	(1)
Stable relationship (> 6 months)		40	25.36	33.2		
No stable relationship		23	33.96	43.0		
Life event (LE) before onset	63				0.268	(1)
LE before first episode		34	25.24	34.2		
No LE before first episode		29	32.14	37.5		
LE during course	63				0.100	(1)
LE during course		50	25.77	35.4		
No LE during whole course		13	39.96	70.7		
Initial episode	63				0.252	(2)
Melancholic		2	9.07	11.5		
Manic		3	31.46	56.0		
Manic-depressive		5	17.61	18.0		
Schizophrenic		9	33.92	45.5		
Schizodepressive		30	33.75	42.5		
Schizomanic		6	21.50	26.1		
Schizomanic-depressive		3	38.88	109.6		
Non characteristic		5	18.65	21.2		
Schizophrenic episode during course	63				0.616	(1)
Schizophrenic during course		17	25.78	26.5		
No schizophrenic episode during course		46	29.16	40.0		
Polarity	63				0.033 *	(1)
Unipolar		31	35.59	45.5		
Bipolar		32	22.52	26.1		
Polymorphism	63				0.322	(1)
Monomorphous		19	33.12	43.0		
Polymorphous		44	26.32	35.4		
Productive psychotic symptoms	63				0.736	(2)
Paranoid		18	29.09	40.0		
Hallucinosis		2	19.17	40.1		
Paranoid-hallucinatory		32	26.39	31.1		
Non productive		11	34.93	45.5		

(1) = t-test; (2) = Anova + Duncan test; * = $P < 0.05$

Table 6. Average length of cycles (log) – correlation analysis (intraindividual mean values). Schizoaffective disorders ($N = 63$)

Variable	Pearson r	Significance P
Age at onset	−0.0932	0.467
Age at follow-up	0.1509	0.238

Table 7. Results of stepwise multiple regression analysis length of first cycle (log), (months). Schizoaffective disorders ($N = 63$)

Dependent variable:	length of first cycle (log)
Independent variables:	age at onset, LE during course, schizodepressive inital episode, schizomanic inital episode, polarity

Variable	Coefficient	β coefficient
Age at onset	−0.0496	−0.4076
LE during course	−0.8946	−0.3030
Schizodepressive beginning	0.7059	0.2801

$R = 0.5925$, $R^2 = 0.3510$, $P = 0.000$, Intercept = 5.6216

Table 8. Average length of episodes (months) (intraindividual mean values). Schizoaffective disorders ($N = 71$)

Median	2.00
$\bar{x}$	2.43
Min.	0.37
Max.	12.00
LN $\bar{x}$	0.51
Geometric mean	1.67
Number of patients	71

patient was excluded) is given in Table 8. Investigating the same factors as for the cycle length (Tables 5 and 6), patients with sthenic, high-self-confident personality had a shorter duration of hospitalization than those with asthenic, low-self-confident personality, and patients with a schizophrenic or schizomanic first episode spent less time in hospital than patients with a schizodepressive initial episode. Patients with a monomorphous course, i.e., only one type of episode during the whole course, also spent less time in hospital ($P < 0.05$).

Stepwise multiple regression analysis showed (Table 9) that the two binary variables schizodepressive first episode and asthenic personality together explained about 20% of the variance. The mean duration of hospitalization associated with each individual type of episode is given in Table 10.

Table 9. Results of stepwise multiple regression analysis average length of episodes (log), (months). Schizoaffective disorders ($N = 63$)

Dependent variable:	Average length of episodes (log)
Independent variables:	Schizodepressive, schizomanic, schizophrenic, initial episode, asthenic personality, sthenic personality, polymorphism

Variable	Coefficient	β coefficient
Schizodepressive beginning	0.3691	0.3011
Asthenic/low-self confident personality	0.3516	0.2821

$R = 0.4434$, $R^2 = 0.1966$, $P = 0.001$, Intercept = 0.1878

Table 10. Duration of hospitalization for every type of episode (397 episodes). Schizoaffective disorders ($N = 71$)

Type of episodes	N (episodes)	$\bar{x}$ (months)
Schizophrenic	29	2.01
Schizodepressive	165	2.90
Schizomanic	76	1.54
Schizomanic-depressive	53	2.42
Melancholic	36	1.86
Manic	12	1.25
Manic-depressive	10	3.22
Non characteristic	7	1.35
Non definable	9	1.80

Table 11. Average length of intervals (months) (intraindividual mean values). Schizoaffective disorders ($N = 63$)

Median	32.21
$\bar{x}$	53.19
Min.	3.62
Max.	212.50
LN $\bar{x}$	3.13
Geometric mean	22.87
Number of patients	63

3.3 Length of the Intervals

An interval was defined as the time between the ending of one episode and the beginning of the next. The length of an interval, like that of an episode, was not precisely definable: cycle length was more reliable.

The mean length of an interval was calculated for each individual patient by adding all the intervals and dividing the sum by the number of intervals (Table 11). For statistical reasons logarithmically transformed values were used. As with the mean length of cycle, the nonintraindividual mean of all 326 intervals

Table 12. Length (months) of interval 1 to 4 in patients having at least 4 cycles ($N = 34$) Schizoaffective disorders

Interval	LN $\bar{x}$	Geometric mean	Median	Paired t-test
1	3.47	32.43	28.75	$P = 0.008$ **
2	2.72	15.19	15.87	$P = 0.971$
3	2.73	15.33	13.25	$P = 0.446$
4	2.54	12.74	12.00	

** = $P < 0.01$

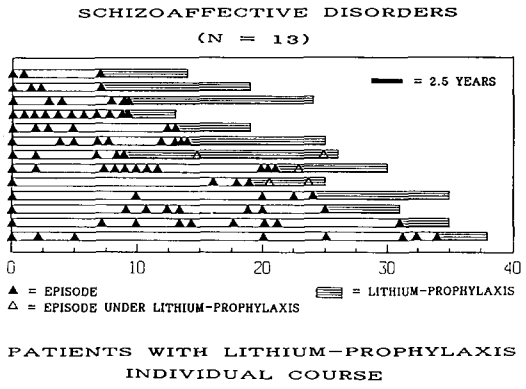

Fig. 3

(median 13.25) implied that the course was much more unfavorable than the intraindividual mean (34.21). Univariate statistical analysis of the logarithmically transformed values (t-test) showed that unipolar schizoaffective disorders had significantly longer intervals than did bipolars. Patients with a melancholic initial episode had a shorter mean interval than patients with a schizophrenic or schizodepressive first episode, but the value of this finding was very limited because only two patients began with a melancholic episode.

The length of the four intervals in the representative population described in Sect. 3.1.1 ($N = 34$) was investigated (Table 12). The length decreased significantly from the first to the second and also from the first to the third ($P < 0.05$) and the fourth ($P < 0.05$) interval. But again, as with cycle length, there was considerable intraindividual and interindividual variation.

3.4 Impact of Treatment and Prophylaxis on Length of Cycles, Intervals, and Episodes

It was decided not to perform statistical analysis of the impact of treatment and prophylaxis on the length of cycles, intervals, and episodes. The reason for this decision was the extraordinary variation in methods and dosages of drugs used. However the individual analysis of each case supported the assumption that prophylaxis with lithium extends the intervals and cycles and sometimes shortens the episodes (Fig. 3).

4. Discussion and Conclusions

Cycle length, i.e., that is the period between the beginning of one episode and the beginning of the next, is one of the most important criterial elements in the course of schizoaffective disorders: Investigation of cycle length is important not only for the prediction of the course but also for prophylaxis and treatment in the intervals between episodes. The length of cycles is a much more reliable criterion than that of episodes and intervals: definition of exactly when an episode begins, and especially when it ends and the interval begins, is difficult if not impossible, particularly if residual symptoms are present. Many symptoms often do not end with an episode, but rather are psychologically interpretable, secondary phenomena caused by the illness, based on the patients' experiences and on the interruption of the continuity of his or her life. The lengths of cycles, intervals, and episodes investigated in the present study were found to be log normally distributed, in agreement with similar previous studies (Angst and Weis 1967; Angst et al. 1973; Angst 1980).

The average cycle length – intraindividually calculated – was found to be 37.5 months (median), very similar to the findings of Angst (1980), who recorded 34.9 months. The investigations of Angst (1980, 1986) showed that cycle length, in schizoaffective as well as in affective disorders, follows some rules. It decreases with increasing number of cycles, a finding confirmed by our present investigation. In particular the difference between the first cycle and the succeeding ones was found to be significant. It has to be stressed, however, that such a model of the course of schizoaffective disorders has only limited validity for individual cases, as there is extraordinary intraindividual and interindividual variation in cycle length.

Bipolar schizoaffective disorders were found to have a significantly shorter average length of cycle than unipolars disorders. Unipolars thus have a significantly more favorable course than bipolars regarding relapse. Although the first cycle was in general the longest, considerable individual variation existed: we found a patient with a very rapid relapse (length of first cycle only 1 month) but also a patient

with a first cycle of 372 months; the second episode following 31 years after the first.

According to the present study, patients with a schizodepressive initial episode, without precipitating factors or with a unipolar course will on average relapse much later after the first episode than those with a schizomanic initial episode, life event, or a bipolar course. Additionally, the older the patient at onset the shorter the first cycle, and so the more rapid the relapse.

The length of episodes found in the present study was shorter than that found in similar investigations (e.g., the Zürich studies). However, this mainly resulted from our decision to define length of episode simply by the duration of hospitalization or inpatient-like treatment. According to our findings, patients with a schizodepressive initial episode needed longer hospitalization than those with schizophrenic or schizomanic first episodes. Also, patients with asthenic, low-self-confident personality stayed longer in hospital than those with sthenic, high-self-confident personality, and patients with a monomorphous course (only one type of episode), stayed longer than patients with a polymorphous course (more than one type of episode).

The decrease in cycle length with increasing cycle number was based on changes in the length of intervals, but not of episodes: the present study showed that the length of episodes was independent from the number of episodes, in contrast to intervals. Bipolars displayed a shorter average interval than unipolars, as was the case with cycles. Our finding that patients with a melancholic initial episode had a shorter mean interval than patients with a schizophrenic or schizodepressive first episode is of very limited value, because only two patients began with a melancholic episode.

In conclusion, the length of cycles and intervals in schizoaffective disorders decreases with increasing number. The difference between the first cycle and the succeeding cycles is significant. Unipolars and patients without precipitating factors have longer intervals. The older the patient at first manifestation of the illness, the sooner the first relapse. Asthenic personalities, patients without precipitating factors, and patients with a schizodepressive initial episode need longer hospitalization.

References

Angst J, Weis P (1967) Periodicity of depressive psychoses. In: Brill H, Cole JO, Deniker P, Hippius H, Bradley BP (eds) Neuro-psychopharmacology. Proceedings of the fifth international congress of the Collegium Internationale Neuro-Psychopharmacologicum, Washington D.C. 1966. Excerpta medica, Amsterdam

Angst J, Baastrup P, Grof P, Hippius H, Pöldinger W, Weis P (1973) The course of monopolar depression and bipolar psychoses. Psychiatr Neurol Neurochir (Amst) 76:489–500

Angst J (1980) Verlauf unipolar depressiver, bipolar manisch-epressiver und schizoaffektiver Erkrankungen und Psychosen. Fortschr Neurol Psychiatr 48:3–30

Angst J (1986) The course of schizoaffective disorders. In: Marneros A, Tsuang MT (eds) Schizoaffective Psychoses. Springer, Berlin Heidelberg New York Tokyo

Angst J, Scharfetter C (1988) Familial aspects of bipolar schizoaffective disorder (in press)

Marneros A, Tsuang MT (1986) Schizoaffective disorders: present level and future perspectives. In: Marneros A, Tsuang MT (eds) Schizoaffective psychoses. Springer, Berlin Heidelberg New York Tokyo

Marneros A, Deister A, Rohde A, Jünemann H, Fimmers R (1988a) Long-term course of schizoaffective disorders. Part I: Definitions, methods, frequency of episodes and cycles. Eur Arch Psychiatr Neurol Sci 237:264–275

Marneros A, Rohde A, Deister A, Fimmers R, Jünemann H (1988b) Long-term course of schizoaffective disorders. Part III: Onset, type of episodes and syndrome shift, precipitating factors, suicidality, seasonality, inactivity of illness and outcome. Eur Arch Psychiatr Neurol Sci 237: 283–290

Tsuang MT, Marneros A (1986) Schizoaffective psychosis: Questions and directions. In: Marneros A, Tsuang MT (eds) Schizoaffective psychoses. Springer, Berlin Heidelberg New York Tokyo

Received March 10, 1988