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Time series models of symptoms in schizophrenia

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Abstract

The symptom courses of 84 schizophrenia patients (mean age: 24.4 years; mean previous admissions: 1.3; 64% males) of a community-based acute ward were examined to identify dynamic patterns of symptoms and to investigate the relation between these patterns and treatment outcome. The symptoms were monitored by systematic daily staff ratings using a scale composed of three factors: psychoticity, excitement, and withdrawal. Patients showed moderate to high symptomatic improvement documented by effect size measures. Each of the 84 symptom trajectories was analyzed by time series methods using vector autoregression (VAR) that models the day-to-day interrelations between symptom factors. Multiple and stepwise regression analyses were then performed on the basis of the VAR models. Two VAR parameters were found to be associated significantly with favorable outcome in this exploratory study: ‘withdrawal preceding a reduction of psychoticity’ as well as ‘excitement preceding an increase of withdrawal’. The findings were interpreted as generating hypotheses about how patients cope with psychotic episodes.

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1. Introduction

Several studies conducted in recent years have shown that time courses of bipolar disorder (Gottschalk et al., 1995; Pezard et al., 1996), schizophrenia (Marengo et al., 2000; Tschacher et al., 1997), and other disorders (Globus and Arpaia, 1994; Bélair et al., 1995; Tschacher, 1996) reveal specific dynamic patterns. The concept of ‘dynamic diseases’ is essential in this respect, suggesting that characteristics of a disorder may not only lie in its structure, its (biological) substrate, but in its

dynamics as well. In the mathematical language of dynamic systems theory (e.g. Kelso, 1995), invariant and stable dynamic patterns are called attractors. As a consequence, the premise of the dynamic disease concept can be sketched briefly as follows: Pathological phenomena are governed by an attractor emerging in a dynamic system; the type of attractor realized in the course of a disorder is, in addition to biological classifications, a potentially essential property of the disorder. Considering the heterogeneity of schizophrenia spectrum disorders, one would expect to find a number of different dynamic patterns.

The objective of the present study was to investigate the dynamic invariants presented in schizophrenia and schizophrenia-like psychotic processes

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soon after the onset of disease. First, descriptions of the dynamic patterns involved in this disorder had to be provided on the basis of empirical data. In a second step consequent to this modeling of the dynamics of psychosis, we wished to assess the relevance of these patterns if they existed. This could be achieved by determining their associations with outcome. The first objective of our study—modeling the dynamic invariants of psychosis—is in line with demands that future research should focus on ‘the interrelationships among the dimensions of the schizophrenic disorders’ (Cuesta and Peralta, 1995). Our study could elaborate on recent findings concerning the dynamic disease concept of schizophrenia (Tschacher et al., 1997; Kupper and Hoffmann, 2000). For this sake we introduced multivariate frequent measurements of symptoms, monitored in a sample of young patients, to examine the temporal associations between the various aspects of psychosis.

At present, relatively little is known about (especially, short-term) associations among psychopathology variables. In spite of a general trend towards dynamic systems approaches in biological as well as behavioral and cognitive sciences, very few empirical investigations have been published to date in this field. An exception is the study of Eaton et al. (1995), who used monthly measurements in a 10-year period finding that positive and negative symptoms were autocorrelated but longitudinally independent of each other. Their finding, however, stands in contrast with reports of notable interrelations between the positive and negative syndromes (e.g. Maurer and Häfner, 1991). Time series modeling of psychosis, especially with real empirical measurements as its foundation, is clearly still in its infancy. This state of affairs influenced the study reported here in two ways: First, we chose daily measurements as our sampling rate because day-to-day variations appeared to be a natural time scale for the modeling of single psychotic episodes. Second, we evaluated simple linear dynamic models in an attempt to achieve a first exploratory approximation to the presumably complex dynamics of schizophrenia.

2. Methods

2.1. Subjects

The sample consisted of 84 treatment episodes generated by 84 patients of the acute ward ‘Soteria’ in Bern, Switzerland (cf. Ciompi et al., 1993). During these treatment episodes the patients were admitted as inpatients of the Soteria ward. Throughout the period of hospitalization, the temporal evolution of psychotic symptoms of a patient was observed. Patients had a mean age of 24.4 years (S.D. 6.0 years). The mean length of the treatment episodes was 91 days (S.D. 51.5 days) documented by daily ratings. Patients had a mean of 1.3 (most frequently occurring score, 0) previous admissions as inpatients. Males accounted for 64% of patients.

The sample was a subgroup of Soteria patients which was selected solely on the grounds of the following two criteria: First, for methodological reasons, the minimum observation period was 20 days; patients with shorter treatment episodes were not considered in this study. Second, only those patients were included who had received an ICD-10 diagnosis of schizophrenia (F20, $n=29$) or schizotypal and acute psychotic disorder (F23, $n=55$). In patients with multiple recorded admissions, the first admission was chosen.

The patients received regular inpatient treatment in the Soteria clinic. Treatment consisted of milieu therapy in a community-based open ward combined with low-dose neuroleptic therapy. Ciompi et al. (1993) reported that the prescription of neuroleptics (chlorpromazine equivalents) in this ward was approximately 50% of that of a matched control group undergoing standard psychiatric treatment. The therapeutic stance was centered on the individual resources of patients rather than their deficits. In general, the treatment philosophy conformed to a holistic and humanistic approach promoting positive affects. The patients were viewed as residents undergoing a period of serious crisis, thus avoiding psychiatric categories and labeling. The ward atmosphere may be described as supportive and tolerant with an emphasis on providing shelter from stressful events.

2.2. Time series data

Ratings of a patient's symptomatology were performed daily by the staff of the ward. The ratings were based on observation, not on a standardized interview. The raters were nurses who interacted closely with the patients during the day. Therefore, their impressions were not merely derived from observation but also from talking with patients about their problems and symptoms, albeit in a non-standardized way. Ratings were always made at the end of the day after work had been completed. The raters were blind to the previous ratings of a patient's symptoms. Each patient was assessed by multiple raters because different nurses were on duty in the course of a patient's stay.

A rating scale was developed especially for these frequent multivariate ratings of psychotic symptoms. This scale was based on the univariate scale described in Aebi et al. (1993) and Tschacher et al. (1997), which had allowed fairly reliable observations (Kendall's tau of 0.70). The new rating scale used in the present study was composed of nine items addressing hallucinations, delusions, derealization, confusion, anxiety, ambivalence, tension, depressiveness, and negative symptoms (reliability and validity assessments are provided below). Each item was quantified by a nine-point Likert scale. In this way, the symptom course for each patient was mapped throughout the period of hospitalization.

2.3. Treatment outcome data

Outcome was assessed by comparing the symptom levels of the initial days of treatment with those of the final days of treatment. This assessment was based on the daily symptom ratings. For each individual course, the outcome measures were defined as follows:

$$ES_x = \frac{\bar{x}_{\text{pre}} - \bar{x}_{\text{post}}}{SD_{\text{pre}}}$$

where ES_x denotes the effect size of variable x (for example, 'hallucinations'), which is defined as the difference of the averages of the initial and final 5 days ($\bar{x}_{\text{pre}} - \bar{x}_{\text{post}}$), normalized by SD_{pre} , the

sample standard deviation of the initial values x_{pre} . In the process-outcome investigation, these effect sizes were the outcome variables to be predicted by the process parameters.

2.4. Time series modeling

As a first preparatory step prior to time series analysis, principal component analysis (PCA) was conducted to test if the nine variables might be reduced to a smaller set of factors. The reason for factorizing the raw data was to achieve a condensed description of the 84 courses which would allow the computation of parsimonious time series models with few parameters. We performed PCA of all concatenated ratings of all patients ($n > 14\,000$), the so-called chained-P technique. The number of meaningful factors was determined with the scree test. A three-factor solution was chosen that accounted for 73.2% of the total variance.

Subsequent varimax rotation grouped the three factors as follows: The factor 'psychoticity' was composed of the ratings of hallucinations, delusions, derealization, and confusion (explained variance: 28.5%); the factor 'excitement' consisted of anxiety, ambivalence, and tension (explained variance: 26.3%); the factor 'withdrawal' included depressiveness and negative symptoms (explained variance: 18.4%). The internal consistency of the three factors as expressed by Cronbach's coefficient was $\alpha = 0.87$ for 'psychoticity' (four items), $\alpha = 0.76$ for 'excitement' (three items) and $\alpha = 0.72$ for 'withdrawal' (two items). Considering the small number of items in the factors, these values corresponded to a good internal consistency. The final values of the factors were computed as the unweighted means of the highest loading items (e.g. 'withdrawal' at day t was defined by the mean of 'depressiveness' and 'negative symptoms' at day t).

Interrater reliability of the factor scores and of the sum of all scales was assessed in an extensive test under naturalistic conditions in the treatment setting. Reliability was calculated using intraclass correlations (ICC) (Shrout and Fleiss, 1979). Weighted values of multiple ICC(2,1) scores were computed. Interrater reliability was $ICC = 0.71$ for the sum score, $ICC = 0.60$ for 'psychoticity',

ICC=0.66 for ‘excitement’ and ICC=0.58 for ‘withdrawal’.

The validity of the daily ratings was assessed by comparing averaged daily ratings with PANSS scores in 25 randomly selected patients. Daily ratings were averaged across a period of one, two and four weeks that preceded the date of the respective PANSS interview. Correlations between these averaged daily ratings and the PANSS scores in general ranged from moderate to high, supporting the validity of the daily ratings. The factor ‘psychoticity’ correlated with the PANSS positive score for all three time periods (Pearson’s $r=0.60$ for one preceding week, $r=0.63$ for two weeks, and $r=0.76$ for four weeks). ‘Psychoticity’ was best described by PANSS P1 ‘delusions’ (validities $r=0.64/0.71/0.76$). The factor ‘withdrawal’ correlated with the PANSS negative score ($r=0.62/0.61/0.57$). This factor captured especially well the PANSS items ‘emotional withdrawal’ N2 (0.73/0.70/0.67), ‘passive social withdrawal’ N4 (0.69/0.67/0.66), and ‘lack of spontaneity’ N6 (0.68/0.71/0.67). The factor ‘excitement’ correlated moderately with the PANSS ‘general psychopathology’ scale (0.50/0.52/0.43). (It should be noted, however, that the correlation between the factor ‘excitement’ and PANSS P4 ‘excitement’ was small. Therefore, these variables have identical labels but must not be considered congruent.)

Time series analysis depends crucially on the stationarity of the courses. A further preparatory step was therefore to ensure stationarity of the data by eliminating statistical trends in the time series of the three factors if present. A filter was implemented (Kupper and Tschacher, 2002) which corrected for the linear, ramp-like trends of the series occurring frequently in the dataset. These trends, of course, reflected the effects of treatment which were expressed in the treatment outcome data described above, but had to be removed for ensuing time series analysis. The filter consisted of an automated iterative procedure: In each course of length N , a time window starting from day 1 to day m was defined (with $10 \leq m \leq N$). In all time windows the ratio of the variance explained by a linear trend to the total variance was estimated separately for each of the three factors (using the procedure AUTOREG in SAS). The time window

m was chosen which yielded the maximum ratio. Then the respective linear trends were removed from the series (see Fig. 1 for an example). An alternative method to make the time series stationary would be to difference the data and compute models composed of differenced factors. Differencing, however, has the disadvantage that all further discussion would have to address the differenced variables (e.g. ‘change in withdrawal’) instead of the observed variables (e.g. ‘withdrawal’) which would have made interpretation more difficult.

In a final step, time series analyses were performed in each of the 84 courses of symptom factors (Fig. 1 depicts one such course). We decided to compute autoregressive models of first order (i.e. lag 1 models) throughout the sample. The reason for modeling all courses in the same way was to ascertain comparability across all courses which is a necessary condition for the aggregation of the models. The AIC criterion of Akaike (1976) is a tool to estimate the optimal modeling order for a given time series. According to this criterion, in a majority of cases (63%) a time series model of first order was most appropriate. In 17% of the courses no lagged model was proposed by the criterion; in 14% (6%) of the courses modeling with time lag 2 (lag 3 or higher) was suggested. In these latter cases, no systematic bias is introduced even if the less optimal model is enforced. We used the procedure STATESPACE of SAS/ETS software (1993) to compute the lag 1 interrelations between factors. Statespace models of lag 1 are equivalent to vector autoregression (VAR) of first order (the method is called vector autoregression because each time step of each course is given by a vector of three symptom factors). In other words, we determined the regressive association of each of the three factors psychoticity, excitement and withdrawal at day $t-1$ with these factors at day t (one day later). Including the three autocorrelations, this yielded $3 \times 3 = 9$ parameters which quantified the strength of these day-to-day interrelations.

At the end of this procedure, 9 parameters for each of the 84 courses were available for further analyses.

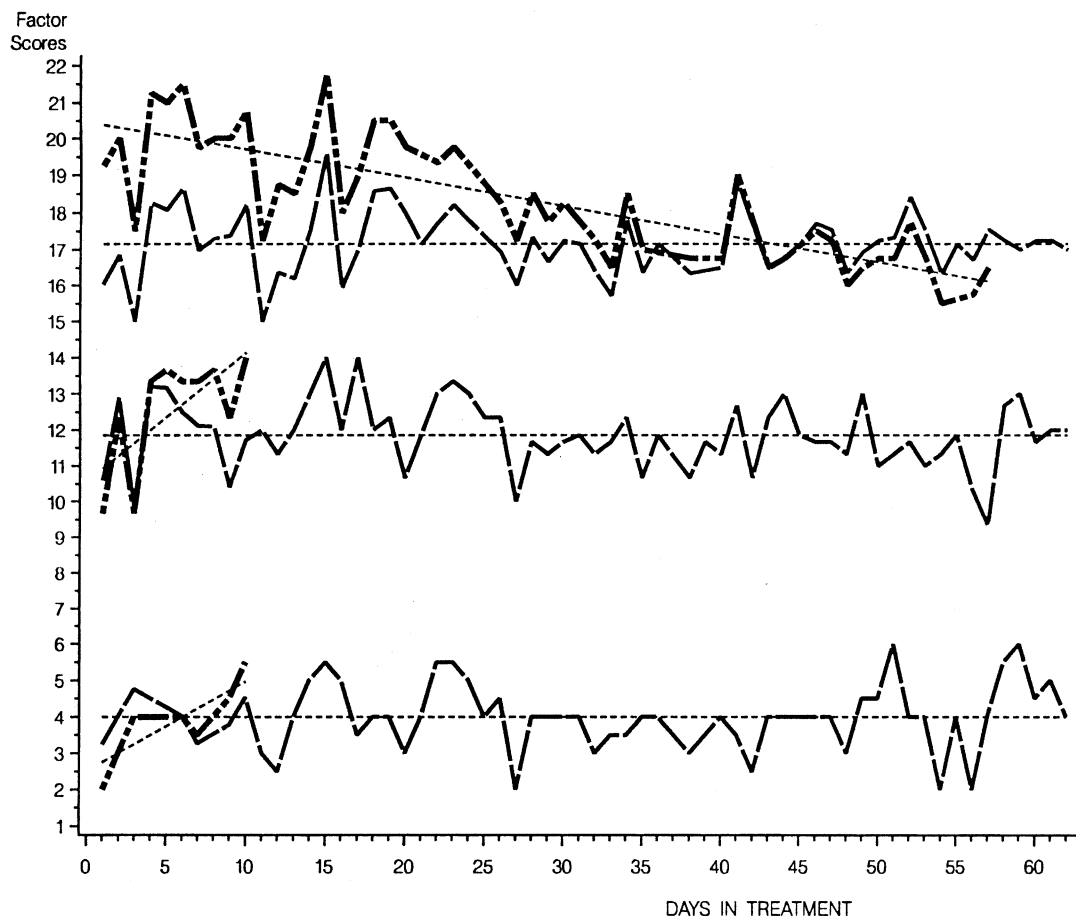


Fig. 1. Symptom course of Pt. 148. From bottom to top: withdrawal, excitement, psychoticity. Corrections for linear trends are shown (see text).

2.5. Process-outcome analysis

The goal of this final step of analysis was to evaluate the association of treatment outcome with process characteristics. The analysis was performed using the time series parameters of all courses (i.e. 84×9 parameters) as predictors in regression analysis. More specifically, this analysis was performed on the *T*-values of all time series parameters (defined as the parameter values divided by their individual standard errors) in order to take into account the statistical impact of each parameter. Treatment outcome was represented by the effect sizes of each single patient. We applied multiple regression analysis to assess the propor-

tion of outcome variance explained by the process parameters. We used backward stepwise regression to indicate which specific parameters were best suited to predict the outcome measures.

Additionally, in order to estimate the association between diagnostic subgroups (F20 vs. F23) and process parameters, we computed a multivariate analysis of variance (MANOVA). The process-outcome analysis and MANOVA were performed by JMP/SAS statistics software.

3. Results

We found a great variety of time-lagged interrelations between psychosis factors in the single

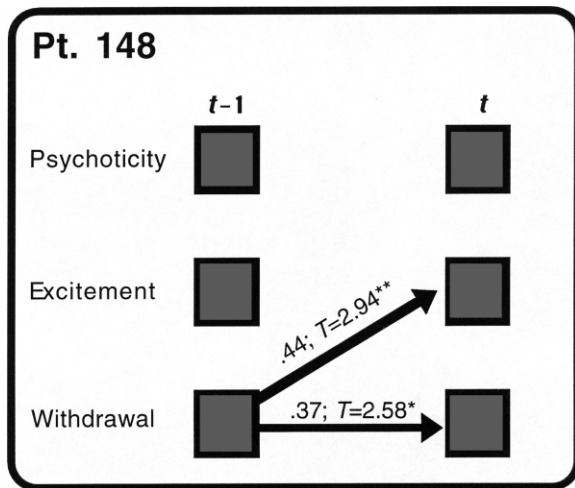


Fig. 2. Individual time series model of Pt. 148 (data see Fig. 1). Arrows starting from the left column (i.e. value at time $t-1$) to the right column (value at time t) indicate significant associations between process variables. The respective weights of the associations and T -values are given (H*; ** symbolize $P < 0.05$; $P < 0.01$).

time series models. Fig. 2 graphs the results of time series analysis of the patient whose symptom course is displayed in Fig. 1. Only the significant interrelations are indicated as arrows in this figure. Positive (negative) variations of withdrawal of the patient preceded corresponding positive (negative) variations of excitement one day later. This patient appeared to react with excitement contingently to variations of withdrawal. Additionally, the autocorrelation of withdrawal was significant.

No single prototypical pattern was found to represent the sample in general. The sample averages of all nine parameters differed from zero significantly, i.e. all process parameters were positively associated with all lagged parameters. The averages and other descriptive statistics of the time series parameters are provided in Table 1. Thus, in this sample, averaging was not a feasible method by which the results of the single time series analyses could be aggregated to characterize the whole sample (but see Tschacher et al., 2000).

The test of differences owing to schizophrenia (ICD-10 F20) vs. other psychotic disorders (ICD-10 F23) showed a significant difference between these two diagnostic subgroups in the whole model

test (MANOVA with d.f. = 8; 75; $F=2.54$; $P < 0.05$). The means and standard deviations of each subgroup and the results of the univariate tests are given in Table 1. The parameter Excitement($t-1$) → Withdrawal(t) was significantly lower in the schizophrenia subgroup.

The degree of symptomatic improvement of the sample was expressed by effect size measures. The mean effect sizes of the three factors as well as the mean effect sizes of the single items of the rating scale are given in Table 2. The reduction of excitement of patients was highest with an effect size of close to 1, i.e. an average improvement by close to one standard deviation.

Yet this study focused neither on the process nor on the outcome of treatment alone, but on associations between process and outcome. In other words, it was tested which specific dynamic patterns (expressed by VAR parameters) were associated consistently with outcome measures (expressed by the effect sizes) using regression analysis. The effect size of excitement was significantly predicted by the set of VAR parameters in the whole model test of regression analysis (Table 3), i.e. one of three main outcome measures was associated with outcome. The significant predictors defined by stepwise regression were Excitement($t-1$) → Withdrawal(t) and Withdrawal($t-1$) → Psychoticity(t).

In addition, stepwise regression analysis was executed for each of the single effect sizes to validate the list of process parameters most relevant to outcome. Table 4 indicates which of the nine VAR parameters were predominantly connected to improved outcome. First, Withdrawal($t-1$) → Psychoticity(t) occurred three times as a significant predictor; a negative beta weight was ascribed to this predictor, i.e. outcome was more favorable in those patients where withdrawal on day $t-1$ ('yesterday') was associated with lower psychoticity on day t . Second, the parameter Excitement($t-1$) → Withdrawal(t) was connected to outcome twice, both times with positive beta. Thus, outcome was also improved when excitement 'yesterday' preceded withdrawal 'today'. In one analysis, Psychoticity($t-1$) → Psychoticity(t), i.e. the autoregression of psychoticity, was found

to be a significant predictor. The weight of this predictor, however, was quite low.

Furthermore, it was found that the residual status of patients' excitement during their final week of treatment was correlated with higher Withdrawal($t-1$) \rightarrow Psychoticity(t) ($r=0.27$, $P=0.01$) as well as with lower Excitement($t-1$) \rightarrow Withdrawal(t) ($r=-0.23$, $P=0.04$). The parameter Psychoticity($t-1$) \rightarrow Psychoticity(t), however, was correlated with the initial values of psychoticity and excitement ($r=0.23$, $P=0.03$ in both cases). Thus, the parameter Psychoticity($t-1$) \rightarrow Psychoticity(t) should not be regarded as a predictor of outcome because no correlation with the endpoint of treatment exists. Autocorrelation of psychoticity therefore is a consequence of initially high psychopathology rather than a predictor of outcome. This correlational finding is reversed for both other VAR parameters highlighted in the regression analysis. The parameters Withdrawal($t-1$) \rightarrow Psychoticity(t) and Excitement($t-1$) \rightarrow Withdrawal(t) are both unrelat-

Table 2
Effect sizes of patients in sample

Outcome factors	Mean E.S. (S.D.)
Factor Psychoticity	0.65 (1.05)
Factor Excitement	0.92 (1.34)
Factor Withdrawal	0.67 (1.31)
Outcome items	
Hallucinations	0.47 (0.90)
Delusions	0.65 (1.02)
Derealization	0.54 (1.11)
Confusion	0.64 (1.18)
Anxiety	0.75 (1.22)
Ambivalence	1.04 (1.43)
Tension	0.62 (1.30)
Depressiveness	0.71 (1.35)
Negative symptoms	0.53 (1.27)

Note. E.S., effect size; S.D., standard deviation.

ed to the psychopathological status of patients during the first week of treatment; they are correlated with psychopathology still present in the

Table 1
Differences in VAR parameters of patients and univariate tests of diagnostic subgroups

VAR parameter	<i>T</i> -values of VAR parameters, complete sample ($N=84$) mean/median (S.D.)	<i>T</i> -values of schizophrenia patients F20 ($n=29$) mean (S.D.)	<i>T</i> -values of psychotic disorders F23 ($n=55$) mean (S.D.)	Univariate <i>t</i> - tests that means of F20 and F23 differ <i>P</i>
Psychoticity($t-1$) \rightarrow Psychoticity(t)	4.48/3.77 ^c (3.67)	4.09 (2.86)	4.70 (4.05)	0.49 ns
Excitement($t-1$) \rightarrow Psychoticity(t)	0.40 ^b /0.43 (1.14)	0.67 (.91)	0.26 (1.22)	0.12 ns
Withdrawal($t-1$) \rightarrow Psychoticity(t)	0.26 ^a /0.23 (1.18)	0.11 (1.40)	0.33 (1.05)	0.41 ns
Psychoticity($t-1$) \rightarrow Excitement(t)	0.67 ^c /0.47 (1.27)	0.99 (1.15)	0.51 (1.31)	0.10 ns
Excitement($t-1$) \rightarrow Excitement(t)	2.99/2.96 ^c (2.23)	3.05 (2.18)	2.96 (2.28)	0.85 ns
Withdrawal($t-1$) \rightarrow Excitement(t)	0.45 ^b /0.34 (1.31)	0.62 (1.57)	0.35 (1.16)	0.38 ns
Psychoticity($t-1$) \rightarrow Withdrawal(t)	0.56 ^c /0.47 (1.37)	0.72 (1.42)	0.47 (1.35)	0.43 ns
Excitement($t-1$) \rightarrow Withdrawal(t)	0.43 ^c /0.49 (1.10)	0.10 (1.06)	0.60 (1.10)	0.049
Withdrawal($t-1$) \rightarrow Withdrawal(t)	3.25/3.02 ^c (2.13)	3.73 (2.34)	2.99 (1.98)	0.13 ns

Note: Test of null hypothesis that whole sample means (resp., for non-normal distributions, medians) differ from zero; ^a $P < 0.05$. ^b $P < 0.01$. ^c $P < 0.001$ (two-tailed). ns, not significant.

Table 3
Process-outcome analysis: multiple regression and stepwise regression analyses for VAR parameters predicting effect sizes of factors

Outcome domain	Multiple regression (whole model)		Stepwise regression (backward)		Significant predictors in stepwise regression model
	R^2	F	R^2	F	
ES of psychoticity	0.10	0.89	0.04	3.51	Excitement($t-1$) \rightarrow Withdrawal(t)
ES of excitement	0.23	2.39 ^a	0.17	8.22 ^c	Withdrawal($t-1$) \rightarrow Psychoticity(t) Excitement($t-1$) \rightarrow Withdrawal(t)
ES of withdrawal	0.10	0.93	–	–	

Note: Dashes indicate that backward stepwise regression analysis could not be performed because all VAR parameters failed to enter the model. $N=84$. ^a $P<0.05$. ^b $P<0.01$. ^c $P<0.001$. ES, effect size. VAR, vector autoregression.

Table 4
Process-outcome analysis: significant predictors for outcome in subscales (backward stepwise regression)

Outcome variable	Stepwise regression R^2	Significant predictors ($P<0.05$)	Estimate of predictor
ES of hallucinations	0.05	Psychoticity($t-1$) \rightarrow Psychoticity(t)	0.06
ES of anxiety	0.13	Withdrawal($t-1$) \rightarrow Psychoticity(t) Excitement($t-1$) \rightarrow Withdrawal(t)	–0.29 0.24
ES of ambivalence	0.09	Withdrawal($t-1$) \rightarrow Psychoticity(t)	–0.37
ES of tension	0.15	Withdrawal($t-1$) \rightarrow Psychoticity(t) Excitement($t-1$) \rightarrow Withdrawal(t)	–0.23 0.36

Note: In 5 of 9 subscales, VAR parameters failed to enter the regression model at significance level. $N=84$. ES, effect size. VAR, vector autoregression.

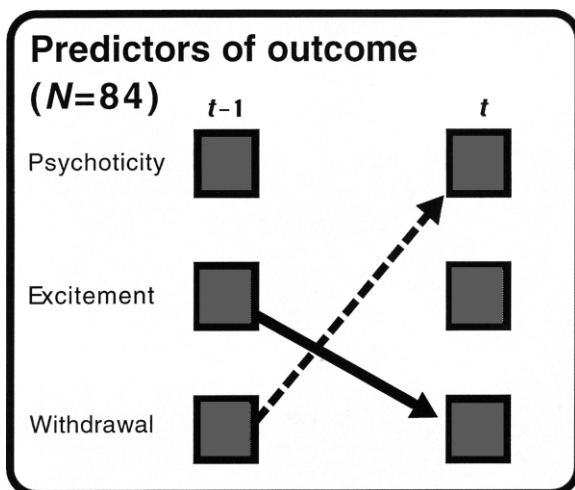


Fig. 3. Graphical display of parameters associated with outcome (predictors) in the sample. Dotted arrow indicates negative association.

final week of treatment right before discharge. Thus these two parameters result from the process-outcome investigation as true predictors of outcome. These predictors are displayed graphically in Fig. 3.

4. Discussion

Analyzing data of systematic daily observations of schizophrenia and acute psychotic courses, we identified substantial autocorrelations and lagged cross-correlations in the process data. Descriptions of the dynamical patterns underlying psychotic disorders could thus be provided for all individual episodes. This stands as an example for the modeling of invariants that is called for by the dynamical disease concept. Consistent with the heterogeneity of schizophrenia spectrum disorders, no single prototypical pattern for the whole sample emerged. There were some differences, however,

between the schizophrenia diagnostic subgroup and the schizophrenia-like psychosis subgroup; but this sign of differential dynamic patterns was considered as weak compared to the heterogeneity of process patterns.

This study represents an exploratory approach to the short-term dynamics of psychopathology, a field where few quantitative studies exist to date. Its exploratory nature is reflected by various points: First, the use of ‘soft’ techniques such as stepwise regression analysis does not allow us to decide between rival hypotheses as an experimental design would. This methodology was used to establish a tentative first step in largely unknown terrain. Second, given the field conditions of the Soteria clinic, potent external variables (‘third variables’) such as medication, life events, family interventions, etc., were not controlled for or randomized. Field studies, however, entail advantages as well as disadvantages: While some variables cannot be controlled, the observations obtained by a field study design are recorded with little obtrusiveness and have high ecological validity. The values of interrater reliability were slightly lower than those usually reported for psychopathology scales such as PANSS, SANS and SAPS or BPRS. This should be viewed, however, in the light that the conventional scales include a large number of subscales—the reliabilities of these subscales are often in the range of the reliabilities reported here. Especially the validities of the daily ratings are remarkably high for measurements in the field. In contrast to Eaton et al. (1995), who found no cross-correlations between monthly ratings of positive and negative symptoms, these were large in our modeling of daily data. This may mean that the time scale of day-to-day variations is a natural time scale that deserves more attention in future research.

Due to the process-outcome results obtained by regression analysis, $\text{Withdrawal}(t-1) \rightarrow \text{Psychoticity}(t)$ and $\text{Excitement}(t-1) \rightarrow \text{Withdrawal}(t)$ were predictive of outcome. Lacking an experimental environment, these dynamic findings must be interpreted with caution. Third variables might distort a coefficient in a time series model. Nevertheless, we hold alternative explanations to be unlikely given the consistent significant findings in this

rather large sample of 84 independent patients who were monitored at over 7000 points of measurement. Therefore, based on the statistics of the time series analyses, one may assume that if some factor A significantly preceded factor B in a time series model, factor A is intrinsically related to factor B; A may even have caused B.

Thus, we may generate the following hypotheses about process-outcome relationships: First, in more favorable courses of disorder, withdrawal was followed by lessened psychoticity. In other words, withdrawal appeared to have a beneficial, damping effect on psychoticity in good outcome patients—withdrawal was antagonistic to subsequent psychoticity. Second, withdrawal was preceded by excitement in favorable courses. This ‘antipsychotic’ impact of excitement may be regarded as indirect in that it alleviated psychoticity via its positive, enhancing association with withdrawal. This effect of excitement on withdrawal was especially high in acute psychosis (F23) patients.

One may speculate that coping mechanisms are reflected in this dynamic structure; the daily variation of withdrawal and excitement represented a beneficial function in the dynamic patterns of symptomatology. The coping capacity of patients is at the core of an integrative view of schizophrenia (Lieberman, 1986). Its varying impact on the course of schizophrenia disorders has been documented by numerous authors (e.g. Böker and Brenner, 1983; Lee et al., 1993; Hoffmann et al., 2000). It may be noted here that coping capacity and self-efficacy are generally regarded as fundamental therapeutic mechanisms in psychotherapy research (Grawe, 1997). Evidence of coping processes in schizophrenia would be of obvious clinical importance because it would suggest a therapeutic use of these processes. In the context of our data, coping with psychoticity might mean that specific psychotic symptoms (hallucinations, delusions, etc.) may be successfully dealt with by less specific emotional and behavioral means as are included in the factors excitement and withdrawal of the present study. If it were possible to implement such mechanisms contingently to prevent or alleviate psychosis in the way shown in Fig. 3, a positive outcome should be enhanced. The assumption, however, that the dynamic pat-

terns indicate coping mechanisms is hypothetical. Experimental designs are needed to support these hypotheses.

Withdrawal, i.e. behavior that was rated by nurses as depressive and negative-symptomatic, signaled the reduction of psychotic symptoms in our data. This finding is consistent with the concept of secondary negative symptoms (Remington et al., 1999; Moeller, 1995) and phasic negative symptoms (Tandon et al., 2000). It is a well-established finding that (primary) negative symptomatology generally antedates the outbreak of manifest positive symptoms in the biographies of persons with schizophrenia (e.g. Maurer and Häfner, 1991). Our data point to a reversal of this pattern in patients who eventually get better—their withdrawal antedates reduced psychoticity. Thus, the present investigation suggests that withdrawal/negative symptoms consist of two components, thereby differentiating the view of the pathognomic nature of the negative-positive sequence by introducing a different time scale—daily fluctuations in contrast to the usually much longer time scales of longitudinal studies in schizophrenia research. We propose that temporal sequences in which withdrawal antedates an increase of specific symptoms of schizophrenia may be related to the general pathological progression of the disorder (Conrad, 1958; Ciompi, 1982), and we wish to add the hypothesis that this progression might be reversed by coping mechanisms on a day-to-day time scale. This would be in line with the finding that phasic negative symptoms are correlated with positive treatment response (Tandon et al., 2000).

What consequences may be drawn from the observed day-to-day dynamics? First, the hypothesis that there are ways by which schizophrenia can be coped with obviously needs more empirical, preferably experimental support. Therapeutic applications such as coping-oriented cognitive-behavioral treatment programs (TARRIER et al., 1993; Schaub et al., 1997; Haddock et al., 1998) would benefit greatly from more precise knowledge of dynamic invariants in psychotic processes. Second, the therapeutic philosophy of the Soteria clinic, where unspecific milieu treatment was provided, may not be as ‘unspecific’ after all. One of its major tenets is that a shielding off from external

stressors has an antipsychotic effect in episodes of psychotic disorder (Ciompi, 1982). The present finding of the effect of withdrawal is clearly in line with this therapeutic guideline.

Our general conclusion is that both schizophrenia research and the treatment of schizophrenia should be ‘dynamics-informed’, i.e. attuned to addressing the underlying dynamics of symptom trajectories. The dynamic view in schizophrenia research may—in the future—help to integrate research approaches which have been pursued quite independently of each other: the longitudinal or epidemiological approach examining time scales of months or years and the clinically based approach that addresses the time scale reflecting one single admission, i.e. days and weeks. One integrating feature of these different research strategies is that sequential patterns of behavior are sought which may characterize schizophrenia spectrum patients as a whole as well as subgroups among the schizophrenia population.

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