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ORIGINAL CONTRIBUTION

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Early-onset schizophrenia

A 15-year follow-up

Abstract The study describes the psychopathological and social outcome of patients treated for schizophrenia in adolescence (mean age at onset 16.0 years/SD 1.52) after a mean follow-up period of 15.4 years (10.2–21.2 years). Out of 55 patients consecutively admitted to hospital, 47 (85 %) could be traced and 39 (71 %) could be re-examined.

At follow-up, 33/39 patients (85 %) had had at least one readmission. Full remission of global psychopathological symptoms [Clinical Global Impression (CGI) ≤ 2] was found in 3/39 (8 %), a moderate outcome (CGI = 3–5) in 22/39 (56 %), and a poor outcome (CGI = 6–8) was seen in 14/39 (36 %). Severe or very severe impairments of global social functioning [Global Assessment of Social Function (GAS) < 51] were observed in 20/39 (51 %). The best predictor of global psychopathological and psychosocial outcome was type of onset (CGI: Beta = 0.36, GAS: Beta = –0.37). A poor outcome was seen in 22 out of 25 cases with insidious onset. All predictors together explained 58 % of the variance in the Positive and Negative Syndrome (PANSS) negative symptom ratings at follow-up. Gender, duration of first inpatient treatment and duration of untreated psychosis were of no predictive value for outcome. The nature of the diagnosis in the first episode strongly predicted the diagnosis given for the whole course after 15 years. In 26/37 cases (70 %), diagnosis at onset and overall diagnoses were the same. Our finding of an incidence of 61 % insidious onset is similar to that in adult onset schizophrenia (AOS), but different to very early onset schizophrenia (VEOS), which shows a higher rate of insidious onset, cognitive impairment and poor outcome. Therefore, it seems that VEOS is a special group compared with early onset schizophrenia (EOS) and AOS.

Key words early onset schizophrenia – adolescent onset schizophrenia – long-term follow-up – prediction – diagnostic stability

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Introduction

There are more than 800 long-term follow-up studies on the course and outcome of schizophrenia (Hegarty et al. 1994), but most of them describe outcome after a relatively short follow-up period (mean 5.6 years), which is too short for a disorder with a chronic or relapsing course. Nearly all of these studies deal with adult onset schizophrenia (AOS).

A comparison of the long-term course of psychopathology in AOS and EOS shows few differences, but EOS may result in a significantly worse psychosocial outcome. An epidemiological study from Eaton et al. (1992) reported that an age of onset under 18 doubles the risk of re-hospitalization in a 3-year period after discharge. Lay et al. (2000) described the psychosocial outcome of EOS after 11 years. They reported 66 % with severe or very severe psychosocial impairment. This rate is significantly higher than in AOS. Thus, illness onset before the age of 18 years is a relevant predictor for psychosocial outcome.

There are also some differences between EOS and VEOS. More than 80 % of children with schizophrenia showed premorbid dysfunction and an insidious onset compared with about 65 % in EOS and adult onset in the studies of Eggers (1973) and Eggers and Bunk (1997). These authors described psychopathological symptoms that were somewhat different from AOS and EOS, for example, acoustic hallucinations that are relatively rare, and coenaesthetic disturbances which seem to occur more often in VEOS than in EOS. However, classification of schizophrenia in children according to DSM or ICD is more difficult than in adults, because children are less able to report subjective symptoms like hallucinations.

A further feature of the course of the illness is whether its nature remains qualitatively the same. Does the diagnosis remain the same and stable over time? Werry (1992) and McClellan et al. (1993) compared the initial diagnoses of schizophrenia in EOS according to DSM-III-R with the diagnoses 3.9 years later and found that only 50 % matched, but Hollis (2000) could confirm initial diagnoses in 41 of 51 cases (80 %) after 11.5 years for EOS.

The present study deals with the course and the outcome of adolescent onset schizophrenia (EOS). The characteristics of premorbid adjustment and of the initial phases of illness are analyzed for their potential as predictors for the outcome of EOS, and the predictive value of the first diagnosis of schizophrenia will be followed up and compared with that 15 years later.

Methods

Subjects

The sample consisted of all patients with a clinical diagnosis of a schizophrenic disorder (ICD-9) consecutively admitted to the Clinic for Child and Adolescent Psychiatry at the University of Essen between 1979 and 1988. Because of the partly unsystematic diagnostic procedures 20 years ago, we included patients with the diagnoses "acute schizophrenic episode (295.4), paranoid syndrome (297.0)" and "non organic psychosis not otherwise specified (298.X)", but affective psychoses (296.X) were not included.

Of these 55 patients, 8 could not be traced or were abroad (3 male/5 female), 4 of the patients and their relatives did not cooperate (1 male/3 female), and 2 of them had died at the time of follow-up. One girl died by suicide, and one boy died during inpatient treatment in a foreign hospital for unknown reasons. One female patient committed suicide during the first inpatient treatment. Of the remaining 42 patients (22 male/20 female), 3 had to be excluded after analysis of the hospital records, as the diagnosis at the index treatment did not coincide with the described symptoms. This left 39 patients in the study (gender male/female, 20/19, and mean age at first admission, 16.9 years; for the group of missing patients, gender male/female, 4/9, and mean age at first admission, 16.3 years). The distribution of the diagnoses schizophrenic, schizoaffective and schizophreniform disorder according to ICD-9 was at admission 31/4/4 and for the missing patients 9/2/2.

Variables and assessment instruments

Hospital records were reviewed by a self-constructed review chart. They consist of five sections: (i) General information (date of birth, gender, age at first admission, diagnosis at first admission, etc.); (ii) Information about the family (parents, siblings, socioeconomic status, etc.); (iii) Anamnestic data (pregnancy, birth, premorbid development, comorbidity, school achievement, etc.); (iv) Symptomatology on admission; and (v) Course of first inpatient treatment. The interrater reliability between two clinical psychologists and two child and adolescent psychiatrists was good (Kappas 0.60–0.95).

We applied the following instruments to assess nine domains of patient features, current and past clinical and psychopathological history. Premorbid adjustment between age 6 and 12 years was rated retrospectively based on hospital recordings and on interviews with patients and parents with the Modified Premorbid Adjustment Scale (MPAS) (Gupta et al. 1995). The scales about withdrawal, peer relationship and interests were rated from 0 to 10, and dichotomized into good (0–6) and poor (7–10) social adjustment. The number of first-degree relatives with psychotic or personality disorder (none vs. one or more) was obtained from the hospital records and semi-structured interviews with the relatives [Structured Clinical Interview for DSM-IV Axis-II (SCID): for psychotic or cluster A Personality Disorder]. Psychiatric disorders in relatives were rated in two steps: (i) by analyzing hospital records. In the review chart, one item asks if any psychiatric disorders are present in first-degree relatives? In 33 out of 39 cases, personal interviews were made with at least one relative; and (ii) in the case of any information about psychiatric disorders in relatives out of these two data sets, additional information was collected either by SKID II interview with the relatives in question or by analyzing the hospital records about inpatient treatments of these persons.

In cases of psychotic disorders, the diagnoses and time of onset were taken out of the hospital records; in cases of possible personality disorders, a SKID II interview was done in order to classify this disorder according to DSM-IV.

Information about the age of onset and course of the symptoms was taken from the hospital records. Additionally, patients and relatives were asked by interview

[Instrument For the Retrospective Assessment of the Onset of Schizophrenia (IRAOS) Häfner et al. 1990] about the time and the abruptness of the initial onset of psychopathological symptoms. The IRAOS is a semi-structured interview for the rating of case-history data and symptoms of the Present State Examination (PSE) (Wing et al. 1974). The time and the course of the initial onset were requested for each of the symptoms. The acuity of onset was scored as '1' for acute (onset of symptoms within 4 weeks), and '2' for insidious (onset of symptoms in more than 4 weeks). All follow-up interviews were conducted by the first author.

An episode of illness was defined as a period of at least 30 days with psychopathological symptoms or a marked deterioration of psychopathology. An episode of illness was defined as psychotic if the psychiatrist who was responsible for treatment at the time classified this period according to ICD-9 as a psychotic episode, or (in two cases) if the symptoms noted reached the criteria for ICD-9 and made this classification possible retrospectively.

The duration of untreated psychosis (DUP) was defined as the period from the onset of first psychotic symptoms until the beginning of the first antipsychotic treatment. It should be borne in mind that fixing the time of onset is possible with greater precision for an acute than for an insidious onset of the illness.

The number and duration of inpatient treatment periods was recorded. The study includes up to eight inpatient treatments for each patient. This led to 175 hospitalizations, of which 160 (91 %) hospital records could be analyzed. The duration of the first inpatient treatment was taken into the calculation as a possible predictor for outcome.

Diagnoses were made at onset, during the course of illness and at the follow-up assessment. ICD-9 diagnoses for the first manifestation and during the further course of illness were taken from the hospital records. The diagnoses at follow-up were given on the basis of the symptoms rated by the interview for Positive and Negative Syndrome (PANSS) (Kay et al. 1989), and made according to DSM-IV. Additionally, an overall diagnosis according to DSM-IV for the whole course was given. The classification was made in a consensus discussion on the basis of the prevailing symptoms during the whole follow-up period.

The positive and negative symptoms at follow-up were rated by PANSS interviews. In 33 of 39 cases, patients were interviewed face-to-face, in 6 cases the parents or close relatives were interviewed. The positive, negative and general psychopathology scales are rated from 1 to 7 (absent to extreme) yielding minimal and maximal scores of 7 and 40 (negative/positive symptoms), and 16 and 112 for the general items. This gives a combined score of at least 30, and maximally 210. The ratings of global psychopathology at follow-up were made with the Clinical Global Impression (CGI) with assessments from 1 (not present) to 8 (extreme). According to the CGI, scores for full remission would be 2, for a partial remission 3–5, and for a severely residual or chronically ill patient 6–8. Lastly, global social function was rated with the Global Assessment of Social Function (GAS) [DSM-IV, AXIS V (APA 1996)], in which severe, moderate and slight impairments are rated < 51, 51–60, and > 60, respectively.

Statistical methods

Data analysis was performed with SPSS 10. Nominal data (gender, diagnostic categories) were tested by Chi-square. Premorbid adjustment and type of onset were dichotomized and also analyzed by Chi-square. The analyses of the possible predictors for outcome were performed by multiple linear regressions. As independent variables we used gender, premorbid social adjustment (PSA), DUP, type of onset, duration of first inpatient treatment and specific psychiatric disorders in first-degree relatives. As dependent variables we analyzed clinical global impression (CGI), psychosocial function (GAS), negative symptoms, positive symptoms, general psychopathology (PANSS).

Results

First admission

The mean age of onset of the first psychotic episode was 16.0 years. Mean age at first admission, which in 33 of 39 cases (85 %) was also the time of the first antipsychotic treatment, was 16.8 years. Mean duration of first inpatient treatment was 182 days (Table 1).

Twelve patients (31 %) had a poor social adjustment between the ages of 6 and 12 years. It is difficult to decide whether this poor adjustment could be seen as a premorbid malfunction or as a very early symptom of the later onset of illness, but there is a significant relationship between this poor adjustment and the type of onset. In general, the ratio of acute vs. insidious onset was 15/24, whereas in the 12 patients with poor PSA the ratio was 1/11 (Chi-square = 5.72/p = 0.02). The rate of poor premorbid social adjustment depended on gender, and was 45 % (9/20) in males and 16 % (3/19) in females (Chi-square = 3.90/p < 0.05).

At the time of first admission, all of the 39 patients lived with their families. In 12 of these 39 families (31 %), there was a first-degree relative with a psychosis [8] or a DSM-IV cluster A personality disorder; in 9 of these 12 cases, the disorder existed already at the time of the first admission; and in 3 cases, a relative became ill between the onset and the patient's follow-up.

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Table 1 Sociodemographic and psychopathological variables in adolescent onset schizophrenia at first admission

Variable	N = 39	(drop-out) N = 13
Male/female	20/19	4/9
Premorbid social adjustment good/poor	27/12	
Type of onset: acute/insidious	15/24	
Age at first onset (mean/SD)	16.0/1.52	
Age at first antipsychotic treatment (mean/SD)	16.8/1.51	
Age at first admission (mean/SD)	16.9/1.4	16.3/3.19
Diagnoses at index-treatment (ICD 9): schizophrenia/schizoaffective/acute schizophrenic episode	31/4/4	9/2/2
Duration of untreated psychosis (days/min/max)	286 (0/1002)	
Duration of first inpatient treatment (days/min/max)	182 (25/853)	151 (35/336)
Psychiatric disorders in first relatives: psychosis/personality disorder (DSM-IV Cluster A)	8/4	

In 14 of the 39 patients, there were one or more definable episodes of psychopathological disturbance which had not been classified as psychotic. The main PSE symptoms of these phases were poor attention, social withdrawal, anxiety, aggressive behavior and sleeping disorders. The relationship between these non-specific symptoms and the later onset of schizophrenia is not clear. These prodromal phases were not included in the DUP analysis. In the first manifestation of psychosis, the main symptoms were delusions, social withdrawal, hallucinations, thought and speech disturbances, sleep disorder and poor attention.

There was no relationship between the psychiatric disorders recorded in the first-degree relatives and gender or PSA of the patients, nor was there a correlation between the type of onset and the age of onset ($t = 0.939$, $p = 0.35$).

Course

In spite of the relatively long duration of the first period of inpatient treatment (182 days), 19 of the 39 patients (49 %) were readmitted within 12 months of discharge. Over the follow-up period of 15 years, only 6 patients (15 %) were not re-hospitalized (Fig. 1).

After the third year following discharge, first re-admissions were rare. Of the 14 re-hospitalizations in the second year, there were only three first re-admissions, the other 11 cases had been re-admitted twice already.

The rate of re-hospitalization varied little over the period of the years 3–10 years following discharge. In the second year after discharge, there were 14 re-admissions; in the third year 9, and in the fourth year this rate increased to 13. In the 10 years following the first inpatient treatment, there was no decrease of the rate of re-hospitalization.

The mean duration of inpatient treatment in the follow-up period was 704 days (min: 59 days, max: 1907 days). This means that EOS patients stayed in a hospital for a duration of nearly 2 years during the 15 years following the first manifestation.

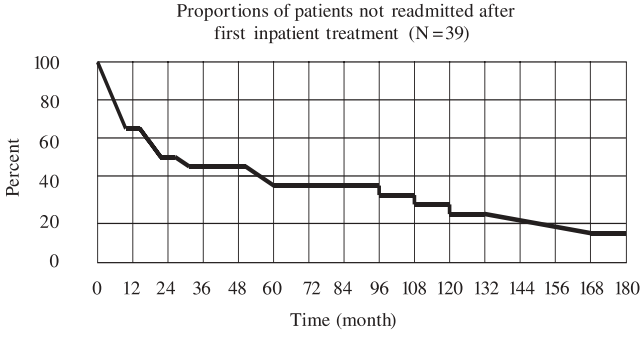

Fig. 1 Rate of readmission in a period of 15 years (180 months) after first discharge in 39 patients with EOS

The diagnoses of 37 out of 39 first manifestations were determined. Table 2 shows the relationship between initial diagnoses and the overall diagnosis for the whole course of illness.

The table shows that in 26 out of 37 cases the diagnosis "schizophrenia" was given at first manifestation. In 23 out of these 26 cases (88 %) this diagnosis could be confirmed at the end of the follow-up period. In two cases the initial diagnosis of schizophrenia was changed to an acute schizophrenic episode, and in one case to a schizoaffective disorder. Two out of three initially diagnosed acute schizophrenic episodes had to be reclassified later to schizophrenia. Two of four patients who were initially classified with schizoaffective disorder obtained an overall diagnosis of schizophrenia at follow-up, the other two cases were confirmed as schizoaffective disorders.

Table 2 Cross-tabulations of the diagnoses at onset (ICD-9) and the DSM-IV overall diagnoses at 15-year follow-up (N = 37)

Diagnosis sum at onset (ICD-9)	Overall diagnosis at 15-year follow-up (DSM-IV)			
	Schizophrenia	Schizoaffective disorder	Schizophreniform disorder	
Schizophrenia	**23**	1	2	26
Schizoaffective psychosis	2	**2**	–	4
Acute schizophrenic episode	2	–	**1**	3
Other	2	1	1	4
Sum	29	4	4	37

Follow-up assessment

The mean age at follow-up was 31.5 years. At this time, psychopathological symptoms, psychosocial function, living situation, financial income, family situation and the state of education and work were assessed.

Psychopathology

In 33/39 cases face-to-face interviews with the patients were carried out, but in six cases only the parents and/or relatives could be interviewed. The nature and severity of the symptoms was assessed with PANSS. Table 3 shows the ten symptoms with the highest ratings.

At follow-up, the residual type of schizophrenia prevailed. Symptoms consisted of reduced social contact, emotional and social withdrawal, reduction of affect, anxiety and tension dominated. There was only one single positive symptom: "Excitement". Thus, the mean sum of negative symptom ratings was significantly higher than that for the score of positive symptoms (24.2 vs. 17.1/t = –5.15, $p < 0.001$).

The global ratings of symptoms with the CGI and the global ratings of the psychosocial functions with the GAS were classified into three categories (Table 4). Three of the 39 patients (8 %) had a full remission (CGI = 2), 22 (56 %) had a partial remission (CGI = 3–5) and 14 (36 %) had a chronic course or no remission (CGI = 6–8). Severe or very severe impairments in several social areas (GAS < 51) were evident in 20/39 patients (51 %). At follow-up, these patients were working in sheltered units or had no structured activity at all. They lived socially withdrawn in institutions or with their parents, without sexual relationships, and were dependent on public or familial assistance. Eleven patients (28 %) still had moderate impairments in at least one area (e. g., rare social contacts, conflicts in school or at work, etc.). Only 8 patients (21 %) had no or little impairment in psychosocial function at follow-up. There were no gender differences on measures of global social function.

Table 3 Rank order of the ten most frequent symptoms in EOS at 15-year follow-up (PANSS rating)

Variable	Mean	SD
N3 Poor rapport	4.36	1.94
N2 Emotional withdrawal	3.95	2.09
N4 Passive-apathetic social withdrawal	3.79	2.09
N1 Blunted affects	3.59	1.92
G02 Anxiety	3.56	2.02
G06 Depression	3.38	1.86
G04 Tension	3.28	1.90
G11 Poor attention	3.26	1.74
P4 Excitement	3.18	1.65
N5 Difficulty in abstract thinking	3.13	1.79

N negative symptoms PANSS (7 items, 1–7); *P* positive symptoms PANSS (7 items, 1–7); *G* general psychopathology PANSS (16 Items, 1–7)

Table 4 Rating of the global remission of psychopathology (CGI) and psychosocial functions (GAS) in 39 patients with EOS at 15-year follow-up

	Frequency	Percent
CGI		
2: Full remission	3	8
3–5: Partial remission	22	56
6–8: Severe residuals/chronic	14	36
Sum	*39*	*100*
GAS		
> 60: Slight impairments	8	21
51–60: Moderate impairments	11	28
< 51: Severe impairments	20	51
Sum	*39*	*100*

In general, there was a close relation between the overall diagnosis across the course and the global psychopathological remission (CGI) at follow-up. Only 5/31 patients (16 %) with an overall diagnosis of schizophrenia were rated as slightly residual (CGI 2–3), while 26/31 (84 %) patients had been classified as moderately to severely ill. On the other hand, the relationship between the initial diagnosis and the global psychopathology at follow-up was less marked. In 9/26 cases (35 %) with an initial diagnosis of "schizophrenia" in the narrow sense of ICD-9 (hebephrenic, paranoid, catatonic, latent and schizophrenia simplex), there were only signs of a slight residuum at follow-up. In this study, a good remission

was observed in 35 % of the cases with an initial diagnosis of VEOS.

Occupational outcome

Of the 39 patients, 6 (23 %) had completed an occupational training and achieved an academic diploma, but 27 (69 %) had not finished any occupational training. At the time of the follow-up, two patients were studying at university, and one patient was working as a non-trained worker. Eight of the 39 patients (20 %) had a regular occupation, 14 (36 %) were working in a sheltered institution or in a rehabilitation program, two (5 %) were working in a clinical setting, and 12 (31 %) were without any structured occupational or educational activity.

Financial situation

Of the 39 patients, 27 (69 %) received public financial assistance, 9 patients (23 %) had an income from regular work (3 male and 6 female), but 4 of the 6 females were married and worked as housewives. The remaining 3 patients received a pension.

Family situation

Twenty-seven patients (69 %) lived alone without a sexual relationship; 12 patients (5 male/7 female) lived together with a partner [5] or in their own family [7]. Although none of the male patients had a child, 3 female patients had one and 2 had two children.

Relations between outcome variables

As expected, there were significant correlations between PANSS sum scores and global ratings with CGI and GAS. Correlations between global psychopathology ratings (CGI) and PANSS "general psychopathology" were $r = 0.87$ ($p < 0.001$), with the scale "negative symptoms" $r = 0.83$ ($p < 0.001$) and with the scale "positive symptoms" $r = 0.76$ ($p < 0.001$).

The correlations between the GAS and PANSS scales were a little lower, but also highly significant [general psychopathology: $r = -0.83$ ($p < 0.001$), negative symptoms: $r = -0.77$ ($p < 0.001$) and positive symptoms: $r = -0.78$ ($p < 0.001$)]. The more severe the symptoms were, the poorer was the psychosocial adjustment.

Predictors

Multiple regression analyses were calculated to find possible predictors for the outcome. As independent variables, we used gender, premorbid social adjustment between the ages of 6 and 12 years, type of onset, duration of untreated psychosis and duration of first inpatient treatment. The age of onset and the number of first-degree relatives with psychiatric disorder were not included, as there were no significant correlations between these variables and any other independent or dependent variables. The dependent variables were the "global rate of remission", the sum scores of PANSS negative and positive symptoms, the total symptom score and the "social adjustment" at follow up. The Beta-weights are listed in Table 5.

There was a significant relationship between type of onset and the severity of symptoms at follow-up. A better outcome and fewer negative symptoms were seen after an acute onset. Additionally, the total sum score of the PANSS at follow-up, including positive, negative and general symptoms correlated with the premorbid social adjustment at age 6–12. With a good premorbid adjustment at this time, there were fewer symptoms at follow-up, but there was no relationship between the positive symptoms at follow-up and any of the variables prior to or at the time of onset.

None of the other predictors explained a significant amount of variance at follow-up. This also holds for the

Table 5 Prediction of clinical global outcome (CGI), psychosocial functioning (GAS), negative symptoms, positive symptoms and general psychopathology (PANSS-sumscore) in early onset schizophrenia at 15-year follow-up. Multiple linear regression analysis

Variable	CGI	GAS	PANSS-symptoms		
			Negative	Positive	Sum
N	39	39	33	33	33
	Beta	Beta	Beta	Beta	Beta
Type of onset	0.36 s	–0.37 s	0.35 s	0.32	0.38 s
Duration of untreated psychosis DUP	0.20	–0.20	0.31	–0.02	0.16
Premorbid adjustment	0.18	–0.09	0.32	0.36	0.41 s
Gender	0.12	–0.08	0.03	0.02	–0.19
Duration of first inpatient treatment	–0.05	0.11	0.09	–0.30	–0.20
R-Square (explained variance)	0.40	0.32	0.58	0.27	0.49
Overall F- test	4.33 vs	3.12 s	7.84 vs	2.08	5.44 vs

s significant ($p < 0.05$); *vs* very significant ($p < 0.01$)

duration of untreated psychosis. There was a significant bivariate correlation between DUP and the outcome variables, but in the multiple regression analysis there was no partial correlation with DUP. This reflects the close relation between DUP and type of onset. With an acute onset, the duration of untreated psychosis was shorter and the outcome at follow-up was better.

Overall, the independent variables explained between 27 % and 58 % of the outcome variance. The amount of variance explained was highest for the negative and lowest for the positive symptoms. There was no relationship between duration of first inpatient treatment and psychopathological outcome at follow-up.

Discussion

This 15-year follow-up study describes onset, course and outcome of adolescent onset schizophrenia in 39 patients. Possible predictors of the course and outcome were investigated.

Limitations

The study was designed as a retrospective follow-up of all patients admitted consecutively to the clinic for child and adolescent psychiatry in Essen with the diagnosis schizophrenia in the 10 years between 1979 and 1988. As the group is relatively small, it may not be representative for all EOS. Gottesmann (1993) estimated that only 80 % of all schizophrenic patients will be admitted to hospital. Thus, there might be a bias towards the selection of the more severe cases.

Data in the hospital records from the early 1980s were used. These were clinical records and not subject to a prospective design. The precision of the retrospective rating of data obtained 15 years previously is limited. The study describes the natural course of EOS without analyzing the effect of different medications or treatments. All follow-up interviews were conducted by the first author. Estimates of the reliability of the symptom ratings by the PANSS interviews cannot be made.

Strengths

Records of the first episode of 37/39 patients (95 %) and the courses of illness, documented by 160 hospital records out of 175 inpatient treatments (92 %), provide a relatively broad and sound database for a long-term follow-up of schizophrenia with an onset in adolescence. Of 39 patients, 33 (85 %) were assessed by personal interviews. It was necessary in only six cases to interview the parents instead of the patients. In addition, the patient interview data were supported by retrospective (IRAOS) interviews with the relatives. Thus, it proved possible to check the reliability of the ratings derived from the patient interviews.

From 55 patients admitted consecutively between 1979 and 1988 and diagnosed with schizophrenia, 47 (86 %) could be traced and only 4/47 (8 %) patients refused to co-operate. These 12 patients did not differ significantly from the study group in the age of onset, gender ratio, and distribution of diagnoses. Thus, no substantial drop-out bias would be expected.

The study presents two main findings: (i) the type of onset is the best predictor of the outcome of EOS after 15 years. The second best predictor is the premorbid social adjustment. There is a close correlation between both variables. For prognosis, the duration of untreated psychosis is of minor importance. Any association is almost completely explained by an interaction with the type of onset; and (ii) the nature of the diagnosis following the first inpatient treatment of EOS is highly stabile across the whole follow-up period of 15 years.

Considering the first finding, the factor "type of onset" was shown to explain 30 % of the total variance of global remission of psychopathology at follow-up. A gradual, insidious onset led to a poor outcome in 22/24 cases (92 %). Only 5/15 cases (33 %) with an acute onset also had a bad recovery. These two groups also differed significantly with respect to social function. There were 17/24 patients (71 %) with an insidious onset, but only 3/15 (20 %) with an acute onset, whose illness deteriorated with a severe or very severe outcome (GAS < 51). Only 2/24 (8 %) cases with insidious onset were either married or lived with partners at follow-up, compared with 9/15 subjects (60 %) with an acute onset.

In general, we found 61 % of patients had had an insidious onset. In adult onset schizophrenia (AOS), the ratio between insidious and acute onset is reported to be nearly the same, but in VEOS the rate of insidious onset appears to be somewhat higher. Eggers et al. (2000) described a rate of insidious onset in VEOS of 72 %, Kolvin et al. (1971) reported an insidious onset of 88 %, and Green et al. (1992) reported a rate of 79 %.

This raises the question: "What is the reason for this age-related type of onset and for the poorer outcome of insidious onset schizophrenia?". Crow (1985) described two types of schizophrenia. Type I schizophrenia with an acute onset, dominating positive symptoms and a good outcome, type II schizophrenia with an insidious onset, prevailing negative symptoms and a poor outcome. He presented some findings for the assumption that type I symptoms are based on a neurotransmitter dysfunction, which can be treated with neuroleptics, and that in type II schizophrenia there are more brain-structural deficits with the consequence of less effect by medication treatment.

Knoll et al. (1998) demonstrated in a longitudinal study with magnetic resonance imaging that there is a

close relationship between ventricular enlargement and age of onset. The earlier the age of onset, the greater the enlargement in the period of 2 years examined. The authors assumed that an insidious onset might be connected with a neurodevelopmental or neurodegenerative brain disorder and a worse outcome.

Consistent with this, Rapoport et al. (1998) reported a high rate of ventricle enlargement in VEOS. They also reported high correlations between ventricle enlargement, premorbid adjustment and severity of symptoms in a 2-year follow-up study.

Our finding of an incidence of 61 % insidious onset is similar to that in AOS, but different to VEOS, which shows a higher rate of insidious onset, cognitive impairment and poor outcome. Therefore, it seems that VEOS is a special group compared with EOS and AOS.

We also observed an interaction between the variables "type of onset" and "duration of untreated psychosis". This means that the duration of untreated psychosis is longer in insidious onset, and that these patients have a poorer outcome. However, this does not mean that there is a poorer outcome because of the longer duration of untreated psychosis. It is likely that the outcome is poor because insidious onset belongs to a different type of schizophrenia with a worse outcome, independent of early or late treatment.

In considering our second main finding, we note that in 26/37 completely documented cases the initial diagnosis (ICD-9) of the first inpatient treatment and the retrospective overall diagnosis (DSM-IV) were the same. The fact that in 23/26 cases (88 %) the diagnosis of schizophrenia after the first admission could be confirmed 15 years later with knowledge of the overall course demonstrates the high predictive value of the initial diagnosis. Over the course of the 10 years following the first admission, with one exception, the only diagnostic changes were within the category of "schizophrenia" (DSM-IV: 295.xx). Further, in 37/39 cases (95 %) such changes of diagnosis referred only to single episodes.

Our findings are in line with studies of the diagnostic stability of EOS. Hollis (2000) found only 20 % of diagnoses of EOS made at 14.2 years of age had changed when followed up 11.5 years later. In this study, the overall diagnosis was also made in a consensus conference, using all available information about the whole course. In our study, it is remarkable that only one case from 39 (3 %) showed a syndrome shift after a period of 15 years. In spite of this high stability of classification, the psychopathological symptoms and the psychosocial development within these classifications were extremely heterogeneous.

There might be two reasons for this contradiction. First, the initial diagnosis was made after the first inpatient treatment. This means after a period of several weeks, and sometimes a month. The mean duration of first inpatient treatment had been 180 days, and consequently these diagnoses can be taken as very reliable. The diagnoses at the following admissions were made in the knowledge of the diagnoses before, as is usual in psychiatric practice. This leads to a high stability for successive diagnoses.

Second, the diagnosis of schizophrenia follows a kind of menu. Sometimes very different and heterogeneous symptom clusters are classified for the same diagnosis. For example, at follow-up many diagnoses had been "the residual type of schizophrenia". This has also to be seen as "schizophrenia", but the symptoms are very different compared to an acute episode. Thus, the symptoms are heterogeneous and variable, but diagnoses in practice are stable.

The heterogeneity of EOS can also be seen in the rate of re-admissions and outcome. There were 19 re-admissions (49 %) from 39 patients within the 12 months following the initial discharge. Only 6/39 patients (15 %) stayed out of hospital for the full follow-up period of 15 years. It is remarkable that the rate of re-admission after discharge remained so stable between 3 and 10 years after first inpatient treatment. There were 11 re-admissions in the eighth and 10 re-admissions in the tenth year. Thus, a significant reduction of the rate of re-hospitalization was not observed. In addition, the mean duration of inpatient treatment did not change in this period, varying between 210 days of inpatient treatment in the fourth year and 75 days in the fifth year without any further reduction over the remainder of the 15-year follow-up period.

It should be noted that the rate of re-hospitalization and the rate of relapse are not necessarily the same. Re-admission depends not only on the course of illness, but also on the availability of familial assistance and the infrastructure of the health system in the area. The high rate of re-hospitalization in this study fits well with the results of other epidemiological studies. Eaton et al. (1992) reported that an age of onset under 18 years doubles the risk of re-admission within 3 years after the initial discharge. More recently, Pencer et al. (2005) also pointed out that the main difference between an AOS and an EOS group followed over a 2-year period after the first episode was the higher rate of relapse in the EOS group. Perhaps the reasons for an early re-admission lie not with a more severe psychopathology in EOS, but the psychosocial vulnerability during this period of development. There are some other features that support this view.

In this study, full remission of psychopathological symptoms (CGI = 2) after a follow-up period of 15 years was observed only in 3 out of 39 patients (8 %). There were 22 cases (56 %) with a moderately residual course (CGI = 3–5) and 22 cases (56 %) with a chronic or severe residual course (CGI = 6–8). There seems to be only little difference between the rate of remission of global psychopathology between EOS and AOS.

However, despite this, schizophrenia with an onset in adolescence led to severe or very severe impairments in psychosocial development (GAS < 51) in 20/39 cases (51 %). In 11 cases there were moderate problems in at least one area of function (e. g., few social contacts, numerous conflicts at school or at work). At the time of follow-up, 15 years after their first manifestation of EOS, these patients worked in sheltered units or they had no structured activity at all. They lived socially withdrawn in institutions or with their parents, dependent on public or familial assistance. Only 8 patients (20 %) had no or mild impairments of social functioning at follow-up.

These ratings of global social adjustment are comparable with those of Lay et al. (2000) using the Disability Assessment Scale (DAS) (Jung et al. 1989). They reported a rate of 66 % for those with severe or very severe psychosocial impairments in a 12-year follow-up of EOS patients. Only 20 % were without any impairments of psychosocial function. In our study, 31/39 patients (80 %) were dependent on treatment or psychosocial assistance at the 15-year follow-up, which is similar to the rate of 75 % reported by Lay et al. (2000) after 12 years. These data confirm the poor psychosocial outcome of patients with EOS. Huber et al. (1979) reported that 39 % of those with an adult onset showed a full social remission, and 18 % a mild residuum after a follow-up period of 22 years. Häfner and Nowotny (1995) suggested that the reason for the poorer psychosocial development of EOS in relation to AOS lay not with the more severe psychopathology, but more with the less psychosocial stability shown at the time of earlier onset. The EOS patient tends to have made no stable relationships, received insufficient education and obtained no remuneration at the onset of illness. These features along with the extraordinarily high rate of re-admission in EOS (which does not merely reflect the degree of psychopathology) support the view that patients with an EOS need intensive psychosocial assistance. Nonetheless, with respect to psychopathology, this study also demonstrated that 58 % of the variance of negative symptoms recorded at 15 years after onset was predicted by the type of onset, duration of untreated psychosis, premorbid social adjustment, gender and the duration of the first inpatient treatment. Therapeutic programs for the treatment of EOS have to consider both of these features.

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