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Epidemiology of early-onset schizophrenia

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Abstract A total of 232 (84%) first episodes of schizophrenia from our epidemiologically defined ABC sample (Age, Beginning and Course) were retrospectively assessed with regard to the onset and early course of the disorder. In a follow-up study a representative subgroup (n = 133) was prospectively examined in five cross sections over 3 years from first admission on. Population-based incidence rates for 5-year age groups comprising a range of <10–<60 years were calculated on the basis of two definitions of onset: first sign of disorder and first psychotic symptom. In 40% of adult patients who had been admitted with a first schizophrenic episode after age 20 years the prodromal phase, in 11% the psychotic prephase, began before that age. This demonstrates that schizophrenia often begins in an age period in which the social and cognitive development and brain maturation are still unfinished. Early-onset schizophrenias (≤20 years) were compared with a medium-onset group (21–<35 years) and a late-onset group (35–<60 years) with regard to age and type of onset, early symptom-related course, social development and social course. The number of schizophrenia-specific positive and negative syndromes in early-onset schizophrenia is comparable to that of higher age groups. However, neurotic syndromes, emotional disorders and conduct disorders are most frequent in younger patients, especially in young men. Paranoid syndromes seem to prevail in late-onset schizophrenia, whereas less differentiated positive syndromes, such as delusional mood, are more frequent in the youngest age group. An earlier onset of schizophrenia has more severe social consequences than onset in adults, because it interrupts the cognitive and social development at an earlier stage. The worse social course of schizophrenia in men compared with women cannot be related to a more severe symtomatology, but to the earlier age at onset and the impairment or stagnation of social ascent at an earlier stage of social and cognitive development. Social disability in the sense of an adaptation to the expectations of the social environment, as well as symtomatology during the further course of schizophrenia, show no major differences between the genders nor between the age groups.

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Introduction

A century ago Kraepelin described dementia praecox as a particular form of dementia beginning at an early age. After clinical observations of late-onset schizophrenia, and of some remitting first episodes without persisting residual syndrome, Bleuler (1911) questioned the appropriateness of the term "dementia praecox" and proposed the more neutral "schizophrenia". Kraepelin followed him in his later publications (1918, 1920). Although an early age at onset has been investigated and confirmed as an indicator of genetic endowment and as a prognostic and pathoplastic factor in several clinical studies, our understanding of the early course of schizophrenia and our knowledge of initial symptoms and types of beginning prior to first contact in particular are still limited. This is true especially for early-onset schizophrenia starting in childhood and adolescence, and for late-onset schizophrenia manifesting after the age of 40 years.

Descriptive epidemiology

Recently, Remschmidt (1988) stated that "representative epidemiological data on the distribution of childhood schizophrenia do not yet exist". He mentioned two reasons for this: firstly, the considerable variability of diagnostic definitions and procedures. He pointed out in his review article that it was not until DSM-III came into use that a clear distinction between early-onset schizophrenia and autism became possible. Secondly, schizophrenic symptomatology tends to be the more varied and non-specific the younger the age of onset. Most epidemiological

studies on early-onset schizophrenia have therefore used the indistinctive and heterogeneous category of childhood psychosis with varying proportions of schizophrenia.

In his own study comprising all types of psychiatric and child-guidance services in three districts of Hesse (Germany) Remschmidt attempted to subdivide childhood psychoses into four diagnostic groups: schizophreniform disorder, affective psychosis, typical non-schizophrenic child and adolescent psychosis and atypical psychosis. He analysed the distribution of age at onset defined by age at first contact for the four diagnostic categories until the age of 15–18 years. As Fig. 1 shows, first contacts for schizophrenia become visible in the age group of 12–15 years, followed by a steep increase in the next age group.

The few studies focusing on age at first contact in early-onset schizophrenia produced similar results (Bleuler 1911; Huber et al. 1975; Gilberg et al. 1986). Gilberg et al. (1986) calculated first-admission rates for childhood psychosis in the age range of 13–18 years on case-register data (Göteborg, Sweden). Their diagnostic category included schizophrenia, schizophreniform disorder, atypical psychosis, affective psychosis and substance-induced psychosis. At age 13 years the rate was 0.9/10,000, showing a steady increase towards adulthood and reaching 17.6/10,000 at age 18 years. A total of 41% of the cases were schizophrenias. In childhood, under the age of 13 years, only two cases of schizophrenia occurred (corresponding to a prevalence rate of 1.8/10,000). Only few authors claim to have identified rare cases of schizophrenia in children aged 4 years or younger (Makita 1966; Kolvin et al. 1971; Vrono 1974). Having observed no onsets of schizophrenia between ages 4 and 9 years, Makita went as far as proposing this age range as a period of latency preceding the onset of schizophrenia. Most authors have expressed serious doubts about the validity of the diagnosis "schizophrenia" at this early age.

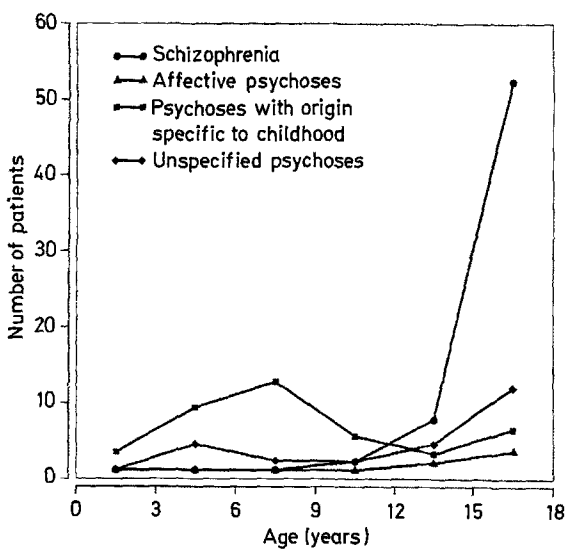


Fig. 1 Age distribution of psychoses in a complete child and adolescent psychiatric utilisation population (n = 3,280) in three districts of the German State of Hesse (Remschmidt 1988)

How to ascertain a diagnosis of schizophrenia in childhood and adolescence?

Precise diagnosis is indeed the main condition for valid epidemiological data on early-onset schizophrenia, but it is more difficult the younger the children assessed. Childhood psychosis presents either multiple or very few symptoms; the most frequent are autism, cognitive deficits, emotional disturbances and conduct disorder. Although transient delusions and negativism with catatonia are occasionally observed in children, a sufficient number of characteristic symptoms justifying a diagnosis of schizophrenia according to the criteria of DSM-III-R or ICD-10 is indeed very rare before the age of 10 years (Stutte and Dauner 1971; Rutter 1972; Beitchman 1985; Remschmidt 1988; Watkins et al. 1988). Eisenberg (1957), Rutter (1972) and Remschmidt (1988) have therefore stressed that the only way of identifying childhood psychosis as an equivalent of schizophrenia in adults is to study its further course. The clinical follow-up studies monitoring childhood psychosis over a period of 10 years or more have yielded very disparate results, because of the differently defined clinical samples used (Kolvin et al. 1971; Jordan and Prugh 1971; Eggers 1978). The only common finding was that only a very small proportion of childhood psychoses actually later develop into schizophrenias. In their follow-up study based on case records and covering 10–11 years, Weiner and Del Gaudio (1976) were able to show that only 62% of the diagnoses of schizophrenia given at ages 12–18 years were confirmed as such in the long-term course. This finding has two implications for the study of early-onset schizophrenia:

1. Due to the low incidence rate sufficiently large populations must be screened for all cases of early-onset psychosis. These cases are followed up for sufficiently long periods of time, e.g. 10 years, with standardised assessment instruments. The disadvantages of this approach are (a) the great effort and expense required and that definitive results are obtainable only after a long follow-up period; (b) missed cases at follow-up assessments may distort the results and (c) the necessity to use a very broad inclusion criterion of childhood psychosis in order not to miss the cases of schizophrenia beginning with non-specific symptoms, a requirement that further raises the costs of such studies.

2. Another approach would be a retrospective investigation of onset and early course in those cases that have developed a reliably diagnosable schizophrenia. This is a considerably less costly method, because the substantial number of childhood psychoses not developing into schizophrenias can be excluded. To ensure that all cases of early-onset schizophrenia are included there must not be any upper age limit for first contact or first admission as usual with samples drawn from child and adolescent psychiatric institutions. Also, cases developing schizophrenia in adolescence, but having their first contact with psychiatric institutions beyond the age of 18 years must be included. A drawback of the retrospective approach is that

recall deficits may lead to inaccuracies in data on symptoms or the time of their appearance.

Collecting data on age of onset and early course

The ideal method of determining the time point of onset of a disorder is a prospective design. But prospective studies are practicable only with illnesses that are frequent enough and start with symptoms observable to the environment such as fever and diarrhoea in cholera. Both requirements are not fulfilled in schizophrenia. It is (a) extremely rare, particularly in childhood and adolescence, and (b) in three-fourths of all cases it starts with non-specific or negative symptoms followed by a prodromal phase of 5 years on average before the first positive symptoms appear (Häfner et al. 1992 a). This means that a retrospective assessment is the only feasible way of obtaining data on the onset of schizophrenia.

The retrospective assessment of onset and early course of schizophrenia has to fulfill the following methodological requirements:

1. The screening procedure used for case finding must ensure the inclusion of all cases, e.g. of non-affective functional psychosis, from a large, epidemiologically defined population.

2. The period of latency between the appearance of first symptoms and the diagnostic interview must be as short as possible to keep recall deficits to a minimum.

3. Age of onset, accumulation of symptoms and type of course must be determined by standardised and reliable assessment instruments.

4. Diagnosis must be independent of interviewer and be given strictly on the basis of the identified symptoms and course characteristics by means of a computer algorithm.

We developed for this purpose a standardised interview (IRAOS; for a detailed description see Häfner et al. 1990, 1992 b) on the basis of internationally approved instruments. It was designed to enable the retrospective assessment of the appearance or persistence of symptoms and behavioural changes as well as of social development within a time matrix. Three sources are used in parallel and independently, i.e. the patient, his closest relative or key informant and written information such as medical records. We administered the IRAOS interviews after remission of the acute episode, i.e. about 6 weeks after first admission, to avoid distortions in information due to acute psychosis. The IRAOS produced data on symptoms and their time of appearance after onset. Also, Present State Examination (PSE) interviews were administered immediately upon admission to assess symtomatology in the acute episode. This data served as a basis for the diagnostic algorithm (CATEGO).

Unlike the usual operationalisations based on first contact or admission, the precise data thus obtained on age of onset allowed conclusions about the beginning of the psychosis in childhood and adolescence and, hence, also a distinction to be made between precursors and early signs or symptoms of the illness. Consequently, it was also possible to distinguish between the consequences of the hidden part of the early course and truly premorbid factors, as demanded by several authors (Aylward et al. 1984; Mednick et al. 1987; Watkins et al. 1988; Shepherd et al. 1989; Crow et al. 1995).

Gender difference in incidence of early-onset schizophrenia

The IRAOS data also provided an opportunity for further analyses: to look into the gender difference in age of first onset. The mean age of onset across the whole age range has been shown to be 3–4 years and, thus, significantly higher for females than males (Häfner et al. 1992 a, 1993 a). However, there is considerable controversy about the question of whether this gender difference is also present in early-onset schizophrenia (Remschmidt 1988). Remschmidt concluded in his review article that most of the relevant studies report higher incidence rates for schizophrenia in boys than in girls. Kolvin (1971) found a ratio of 2.5 to 1 up on analysing early childhood psychosis (in a hospital population up to 15 years of age). Beitchman's (1985) reanalysis of nine studies yielded a gender ratio of 1.75 boys to 1 girl (mostly 5–15 years of age).

The gender ratio naturally depends on the age range of the study population, which, if stated at all, varies from study to study. The upper limit ranges from prepuberty (12 years: e.g. Green et al. 1984; 10 years: e.g. Watkins et al. 1988) to 19 years ("adolescent onset"; Apter et al. 1991). Some other studies did not find any clear gender difference in first admission rates for child and adolescent schizophrenia. Apter et al. (1991), for example, reported a ratio of 51% of boys to 49% of girls in the age range of 12–19 years. Blanz et al. (1995) found similar results with 54% of boys and 46% of girls in the age range of 11–18 years. Galdos et al. (1993) found a slight preponderance of girls in adolescence, but a clear predominance of boys in the preceding and the following age ranges. The validity of the results from the studies mentioned is limited by problems of representativeness of the samples or the fact that the comparisons were based on clinical samples and not on population-related rates for each age group.

The often, but inconsistently, reported reverse gender difference in early-onset schizophrenia, found particularly in first-admission samples from child psychiatric institutions with an upper age limit of 16 or 18 years, reflects the epidemiology of abnormal behaviour in this period of life: at ages 12–25 years boys tend to show considerably more conduct disorders and antisocial behaviour than girls (Esser et al. 1992). The same is true for the early stages of schizophrenia. Socially negative behaviour is highly significantly more frequent in young male than female schizophrenics at first admission (Häfner et al. 1993 a). Due to their dissocial or antisocial illness behaviour a small proportion of young schizophrenics comes first in contact

with youth services and juvenile courts instead of psychiatric services, as shown, for example, by the Los Angeles County Study conducted by Asarnow (1995). In our own sample we had a particularly striking case: a boy who already showed emotional disturbances, conduct disorders and various delusions in elementary school, and a history of dissocial behaviour and increasing problems of social adaptation thereafter. At the age of 23 years and again at 25 years, he was sent to prison for 6 months. It was not until the age of 30 years that he received a psychiatric diagnosis, and at the age of 31 years he was finally hospitalized for schizophrenia.

Epidemiological studies of early-onset schizophrenia based exclusively on utilization data of child psychiatric services therefore run the risk of missing a proportion of male schizophrenics of this age. The consequence are incidence rates artificially shifted to the advantage of females in this age range. If the screening sample covers the total age range, also those (mostly male) early-onset schizophrenics in contact with youth services, juvenile courts or without any professional care in adolescence are probably included.

Early onset: a predictor of an unfavourable course?

Findings on the prognostic value of early onset are inconclusive, probably because of the great methodological problems involved. Studies showing early onset to be a predictor of an unfavourable social and symptom-related course predominate (Eisenberg 1957; Kydd and Werry 1982; Retterstøl 1987). Eggers' (1985) conclusion that "the prepubertal forms of schiozophrenia (10–14 years) do not differ prognostically from the adult-onset type", although based on a review of all the studies thus far published, is in discrepancy with the results of a majority of the studies on the topic. His own long-term study conducted among 57 schizophrenics aged 7–13 years showed that only onset before the age of 10 years was clearly associated with an unfavourable outcome (Eggers 1978).

Studies on early-onset schizophrenia have tended to focus on the disease itself, thus largely ignoring the probably crucial aspect of individual development and its association with the course of the disorder. For example, most studies have failed to consider the possibility that onset of schizophrenia early in social biography might impede ascent to an expected socio-economic status with the consequence of a lower level of social development than if onset had occurred later. Several authors have recently stressed the importance of a clear distinction between symptom-related and social course in order to be able to understand the processes bringing about the social consequences of the disorder (Strauss and Carpenter 1972; Jablensky et al. 1980; Biehl et al. 1986; Shepherd et al. 1989). However, it is also necessary to distinguish between social disability determined by disease-related or environmental factors as a social characteristic of the individual and social-status or social-class variables as characteristics of the patient's objective social situation.

Studies indicate that, unlike the social course, the symptom-related course of early-onset schizophrenia does not seem to differ from that in adult-onset schizophrenias (Remschmidt et al. 1991). It was found for both adult (Marneros et al. 1988; Angst et al. 1989; Huber et al. 1975) and adolescent schizophrenics (Remschmidt et al. 1991) that the pattern of symptoms changes after the remission of the acute episode, positive symptoms decreasing and negative symptoms remaining the same or even increasing in frequency.

Topics and hypotheses

The major topics of the epidemiology of early-onset schizophrenia can be subsumed under cross-sectional and course-related aspects:

Cross-sectional topics

1. Frequency of schizophrenia onset (incidence rates) in a period of life of uncompleted social, cognitive and brain development
2. Age and gender distribution of first onset
3. Initial symptoms of schizophrenia and their association with age and gender

Course-related topics

1. Early course of schizophrenia from onset to first contact; accumulation of symptoms and types of early course (acute, subacute and insidious)
2. Influence of age and gender on the type and symptomatology of early course
3. Premorbid social disadvantage vs social consequences of early course and their effect on the later course of schizophrenia; prediction of long-term course and outcome from the level of social development at onset with reference to age and gender

Study sample

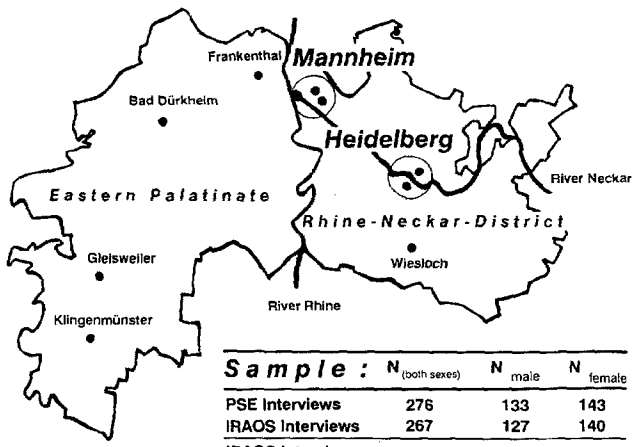
The catchment area of the ABC Schizophrenia Study (Age, Beginning and Course; Häfner et al. 1992a) with a population of about 1.5 million comprises the cities of Heidelberg and Mannheim (Germany) with their surrounding regions (Rhine-Neckar district and eastern Palatinate) depicted in Fig. 2. About half of the population is urban, and the other half is rural. Over a 2-year period (1987–1989) all first admissions for a diagnosis of schizophrenia or related disorder (ICD-9 295, 297, 298.3, 298.4) of German-speaking inhabitants from the catchment area to one of the ten adult and child and adolescent psychiatric hospitals and units of the area were registered.

Inclusion Criteria: first admission in one of the 10 psychiatric hospitals or units

Clinical diagnosis: (ICD-9: 295, 297, 298.3, 298.4)

Exclusion Criteria: organic psychosis, severe mental retardation

Age: 12 - 59 years



Sample :	N (both sexes)	N male	N female
PSE Interviews	276	133	143
IRAOS Interviews	267	127	140
IRAOS Interviews first episode	232	108	124

Fig. 2 Age, beginning and course (ABC) first-episode sample (catchment area of Rhine-Neckar district and eastern Palatinate; approximately 1.5 million inhabitants)

Inclusion criterion was age 12–59 years at first admission for schizophrenia. First admissions at ages 0–11 years were excluded because of their extremely low frequency and the aforementioned uncertainties involved with a diagnosis of schizophrenia in this age group. The sample has been described in greater detail elsewhere (Häfner et al. 1994). A total of 276 patients (143 females and 133 males) were administered PSE interviews (Wing et al. 1973) immediately upon admission – within a week at the latest – and thus mostly in a psychotic episode and assigned to a diagnosis according to the CATEGO algorithm. Onset and early course until first admission were documented by means of IRAOS interviews administered on average within 6 weeks of admission (mostly after remission of the psychotic episode). In this way not only the type and chronological order of symptom accumulation as well as the social biography of the patient, but also possible psychotic episodes before the index episode were ascertained. A psychotic episode was defined by the DSM-III-R criteria for schizophrenia and schizophreniform disorder. Temporal aspects of some criteria that might distort the results, such as persistence of symptoms for 6 months in DSM-III-R, were ignored for methodological reasons. Of the total interview sample, 232 (84%) were first-episode cases (108 males [81%]; 124 females [87%].

Onset and early course until first admission were studied in the first-episode sample. Further course was assessed in a representative subsample of 133 (65 females and 68 males) of the ABC sample at four further waves, 6 months, 1 year, 2 years and 3 years after first admission, with the same instruments.

Onset

The following four definitions of onset were used: points in time when the first signs of the disorder, first positive symptom, maximum of positive symptoms (climax of first episode) and first admission occurred. The sections between these events were termed prodromal phase, psychotic prephase and period of latency (Fig. 3). Discovering that three-quarters of all schizophrenias begin with non-specific or negative symptoms difficult to distinguish from similar symptoms in other mental disorders or from precursors of schizophrenia, we applied a phase model to the first three definitions of onset (Häfner et al. 1994). It is based on the different specificities of the three symptom categories: non-specific symptoms qualified as first signs of the disorder if they were continuously present until the maximum of psychotic symptoms, i.e. the first psychotic episode. Negative symptoms as defined in the PSE were included if they were either continuously present or recurring until first admission. Positive symptoms, such as delusions and hallucinations, were registered in any case, even if they had occurred only once and had temporarily remitted (Häfner et al. 1992).

Completion of age 20 years was chosen as the age limit between childhood and adolescence on the one hand, and the beginning of adulthood on the other, because brain maturation is completed at about that age. Table 1 shows the proportions of cases across the age range for males and females whose first admission, first psychotic symptom and first sign of mental disorder had occurred before age 21 years. Of those cases of the first-episode sample hospitalised for schizophrenia for the first time at adult age, i.e. after age 20 years ($n = 205$; 88%), in 40% the prodromal phase and in 11% the first psychotic episode had started before the age of 21 years, i.e. in childhood or adolescence. The result makes plain the methodological issue discussed at the outset that a considerable proportion of early-onset cases are bound to be missed when samples recruited from child and adolescent psychiatric services with the inclusion criterion of age under 19 years are used. It further suggests that schizophrenia is primarily a disorder of young age, and that adolescence is a relevant risk period of onset.

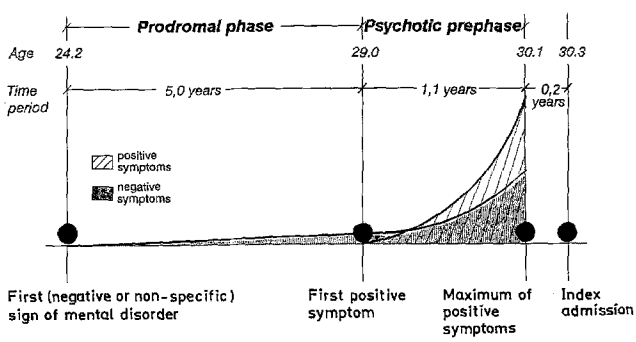


Fig. 3 Prephases of schizophrenia from first sign of mental disorder to first admission

Table 1 Percentages of first onset before age 21 years by three definitions in total first-episode sample

Events of early course as definitions of first onset	Total		Males		Females		m/f ratio
	n	%	*n*	%	*n*	%	
Total first-episode sample	232	100	108	100	124	100	0.9
First admission for a diagnosis of schizophrenia < age 21 years	27	12	16	15	11	9	1.5
First psychotic symptom < age 21 years	49	21	28	26	21	17	1.3
First sign of disorder < age 21 years	109	47	57	53	52	42	1.1

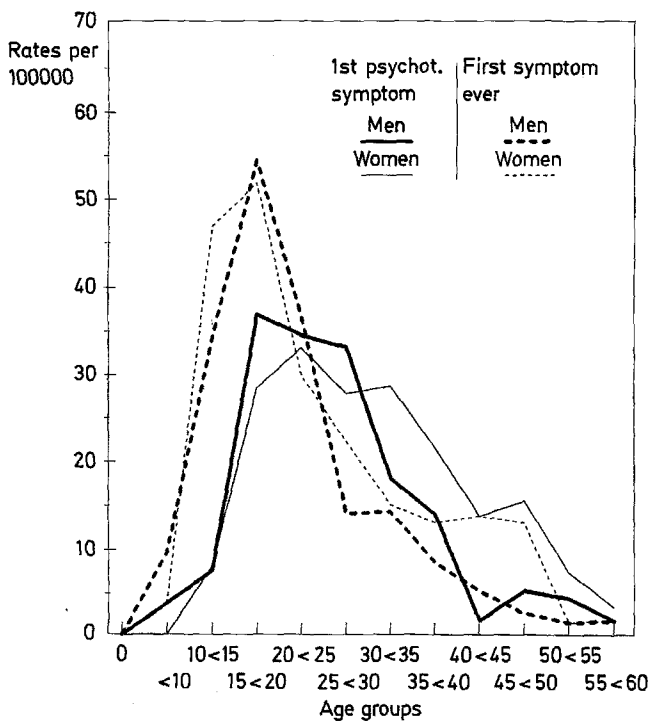


Fig. 4 Onset of first psychotic symptom and first symptom of the illness for different age groups (rates are projected for the entire sample of first admissions per year)

The population-based incidence rates for 5-year age groups in the age range of under 10 to under 60 years by two definitions of onset, first sign of disorder and first psychotic symptom, revealed a steep increase which starts in the youngest age group and peaked between ages 15 and 20 years (Fig. 4). The increase in onsets defined by first psychotic symptom followed with a delay of several years the increase in onsets defined by beginning of the prodromal phase. A clear gender difference became visible, with women showing a higher age of onset with a second peak between ages 45 and 50 years. When the mean age of onset across the total age range was compared between males and females, a significant difference emerged: women were about 3–4 years older than men at first onset irrespective of how it was defined (Häfner et al. 1993).

In several sub-studies we succeeded in explaining this difference and detecting the underlying pathophysiological mechanisms (Häfner et al. 1993). Estrogens seem to reduce the sensitivity of the D_2 receptors in the brain, and in so doing seem to raise the vulnerability threshold for schizophrenia. When the protective effect of estrogens starts to wane in menopause, those women genetically predisposed to schizophrenia, but until then protected from falling ill by the vulnerability-decreasing effect of estrogens, finally develop the disease.

Comparison of early, medium- and late-onset schizophrenia

We compared symptomatology, social development and early course in the three groups: early-onset schizophrenia, medium- and late-onset schizophrenia. For this purpose we divided the first-episode sample of 232 into three age groups by using age at the beginning of the first psychotic episode, i.e. at the appearance of the first psychotic symptom, and age at the appearance of the first sign of the disorder (beginning of the prodromal phase) according to our phase model as a basis.

Table 2 shows a tendency towards more early-onset schizophrenias among males and considerably more late-onset schizophrenias among females for the two definitions of onset. However, the significantly lower average age of onset in males is to some extent masked by the fact

Table 2 Gender distribution in three age groups ($n = 232$)

Age at onset	Definition of onset							
	First sign of illness				First psychotic symptom			
	Total	Males	Females	m/f ratio	Total	Males	Females	m/f ratio
<21 years	109 (47%)	57 (52%)	52 (48%)	1.1	49 (21%)	28 (57%)	21 (43%)	1.3
21–35 years	90 (39%)	41 (46%)	49 (54%)	0.8	136 (59%)	65 (48%)	71 (52%)	0.9
36–60 years	33 (14%)	10 (30%)	23 (70%)	0.4	47 (20%)	15 (32%)	32 (68%)	0.5
Total	232 (100%)	108 (47%)	124 (53%)	0.9	232 (100%)	108 (47%)	124 (53%)	0.9

that the age criterion "<21 years" is close to the age group in which female onsets peak as well. In the total first-episode sample ($n = 232$) mean age at the first sign of the disorder was 25.4 years for females and 22.5 years for males ($P < 0.05$).

Symptomatology at first admission

Symptomatology at first admission was compared on the basis of PSE/CATEGO total scores and the syndrome scores DAH (delusional and hallucinatory syndromes), BSO (behavior, speech and other syndromes), SNR (specific neurotic syndromes) and NSN (non-specific neurotic syndromes; Table 3). The total scores showed a significant difference: The symptom scores fell with increasing age. The highest total scores were found in the early-onset group. An analysis at the level of the four PSE syndrome scores showed that the share of the schizophrenia-specific DAH and BSO scores in the elevated total score of the early-onset group was minimal and not significant. To a much greater extent the excess in the total score was accounted for by highly significantly elevated SNR scores and slightly elevated NSN scores. This finding reflects the clinical impression that early-onset schizophrenias are characterized by a high frequency of non-specific symptoms, apparently attributable to the diagnostic categories of neurotic and conduct disorders. At the early stages of schizophrenia children and adolescents consequently show mainly emotional and behavioural disorders and disturbances in inter-personal relationships. But there was a marked gender difference. Analysis of variance with gender and age yielded a main effect of gender, which attained a statistical trend ($P < 0.1$), and a significant interaction between gender and age, i.e. boys showed significantly higher NSN syndrome scores than did girls. In higher age groups, however, this difference disappeared. No gender differences were observed in the other syndrome scores.

At the level of individual symptoms social anxiety, panic attacks, histrionic behaviour, delusions of reference – but also loss of interest, obsessional ideas and rumination, drug abuse and dissocial behaviour – were significantly more frequent in the youngest group. We suppose that the particular character of this age-related symptomatology might, at least to some extent, not be a direct expression of the disease process, but an age-specific response pattern of personality also encountered in other mental disorders at an increased frequency in this age range. Schizophrenias beginning in a period of life in which personality is not yet fully developed probably trigger response patterns specific to that developmental stage. In late-onset schizophrenias beginning after brain maturation the response pattern involves less symptom and behavioural patterns belonging to earlier stages of brain and personality development. Early-onset schizophrenia probably impedes not only social and personality development, but also the acquisition of adequate communicative competence. However, we could not yet address this question in our study. Negative symptomatology, present in all age groups in the same form and almost at the same frequency, seems to be less dependent on the developmental stage. It is probably a more direct expression of the biological disease process than are positive symptomatology and behavioural abnormalities.

Epidemiology of course and outcome

These results prompted us to direct our research interest to the much-neglected early course of schizophrenia extending from the occurrence of the first sign of the disorder until the climax of the first psychotic episode or first admission.

To classify type of onset we used three notions from the clinical tradition to distinguish different lengths of the prephase from the first sign of the disorder to the maximum of psychotic symptoms acute: 4 weeks or less; subacute: from 4 weeks to 1 year; insidious: more than 1 year). A majority of the cases showed an insidious (68%), 18% an acute and 15% a subacute type of onset. Type of onset did not differ between the age groups.

Table 3 Symptomatology at first admission (first episode sample $n = 232$): syndrome scores and CATEGO total score. DAH delusionary and hallucinatory syndrome; BSO behaviour, speech and other syndromes; SNR specific neurotic syndrome; NSN non-specific syndromes

Symptomatology	At first psychotic symptom			
	<21 years	21–35 years	36–<60 years	ANOVA[a]
DAH	11.2 (7.1)	10.3 (7.03)	10.1 (7.05)	$P < 0.7$
BSO	8.7 (4.1)	7.8 (3.9)	7.4 (5.4)	$P < 0.4$
SNR	9.6 (5.6)	6.7 (4.8)	6.6 (5.5)	$P < 0.003$
NSN	16.3 (9.0)	15.5 (6.3)	13.3 (7.1)	$P < 0.08$
Total score	45.9 (18.7)	40.4 (15.0)	37.7 (16.9)	$P < 0.03$

[a] For three age groups

Table 4 Initial symptomatology in three age groups

	Age (years)	N	Started with positive symptoms	Started with both symptoms	Started with negative symptoms
First sign	<21	109	7 (6%)	92 (84%)	10 (9%)
	21<36	90	7 (8%)	59 (66%)	24 (27%)
	36<60	33	1 (3%)	19 (58%)	13 (39%)
					$P < 0.001$
First psychotic symptom	<21	49	7 (14%)	32 (65%)	10 (20%)
	21<36	136	7 (5%)	105 (77%)	24 (18%)
	36<60	47	1 (2%)	33 (70%)	13 (28%)
					$P < 0.1$
Total group		232	15 (6%)	170 (73%)	47 (20%)

A comparison of initial symptoms, i.e. onset with positive vs negative and non-specific symptoms vs onset with both positive and negative symptoms, across the three age groups showed a clear predominance of negative symptoms. In the youngest group negative initial symptoms were particularly frequent (Table 4).

Accumulation of symptoms in the prodromal phase and the psychotic prephase of schizophrenia

The 18 positive, 13 negative and 35 non-specific symptoms from the IRAOS were analysed on the basis of PSE items as simple additive scores per year for 15 years to 1 year before first admission and per month in the last year preceding first admission (Fig. 5). The mean symptom scores depicted across the years and months studied showed almost exponential increases in all three symptom categories. Positive symptoms, as expected, appeared with a delay of several years, but increased as steeply as non-specific symptoms and clearly more steeply than negative symptoms in the year preceding first admission. Compared across the age groups, positive and non-specific symptoms started to increase earlier in the early-onset group. With regard to the course and steep accumulation of negative symptoms in the first psychotic episode, no differences between the age groups emerged.

Disease course and social development (the impact of onset on social biography)

We were able to show (Nowotny et al. 1995) that the early stages of the disorder and the time point when the disorder

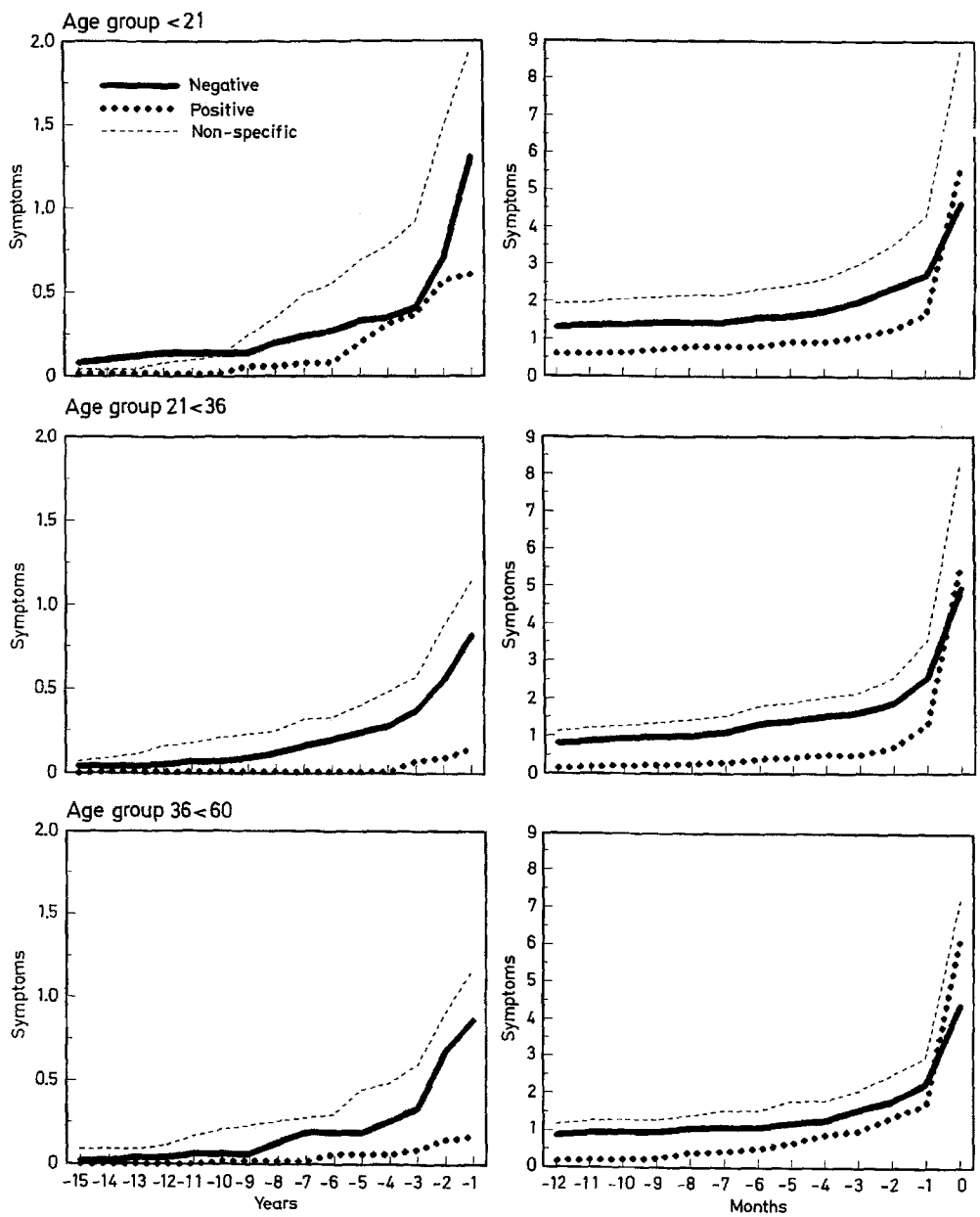


Fig. 5 Accumulation of symptoms per year *(left)* and months (last year – *right*) up to index admission. Age groups according to first psychotic symptom

starts to disrupt social biography have a decisive effect on further social course in adult-onset schizophrenia for at least some years after first admission. Hence, it was all the more likely that onset in childhood and adolescence, i.e. in a period of unfinished personality, cognitive and social development, is bound to have more severe consequences than onset later in life when both personality and socio-economic status have reached a certain stability.

We further tested whether early-onset schizophrenia, due to its disruptive effect on cognitive and social development and by impeding expected social ascent, might have more severe social consequences than later-onset schizophrenia. The earlier age of onset in men and the slight preponderance of schizophrenic boys over girls before age 21 years called for testing the hypothesis that a lower level of social development at onset in males leads to a worse social course of schizophrenia compared with females.

We related three milestones of the early course of schizophrenia – first sign, first psychotic symptom and first admission – to the patients' social biographies as defined by six social-status components. As the comparison of fulfilled social roles across the three age groups demonstrates (Fig. 6), the early-onset group, as expected, showed the lowest number of fulfilled social roles (finished school education, finished occupational training, own income, employment, independent living, marriage or stable partnership) for any definition of onset.

In contrast, the late-onset group (>35 years) showed considerably better social-role fulfillment, attaining values ranging from just under 75% to 90% with more for finished school, job, own income and independent living. The medium-onset group (21–35 years) occupied an intermediate position. A striking finding were the exceptionally low values for marriage and partnership, which even in the highest age group varied only around 60%.

Our results hence show that schizophrenics falling ill before age 21 years significantly lag behind those with later onset in terms of all the social roles analysed – with

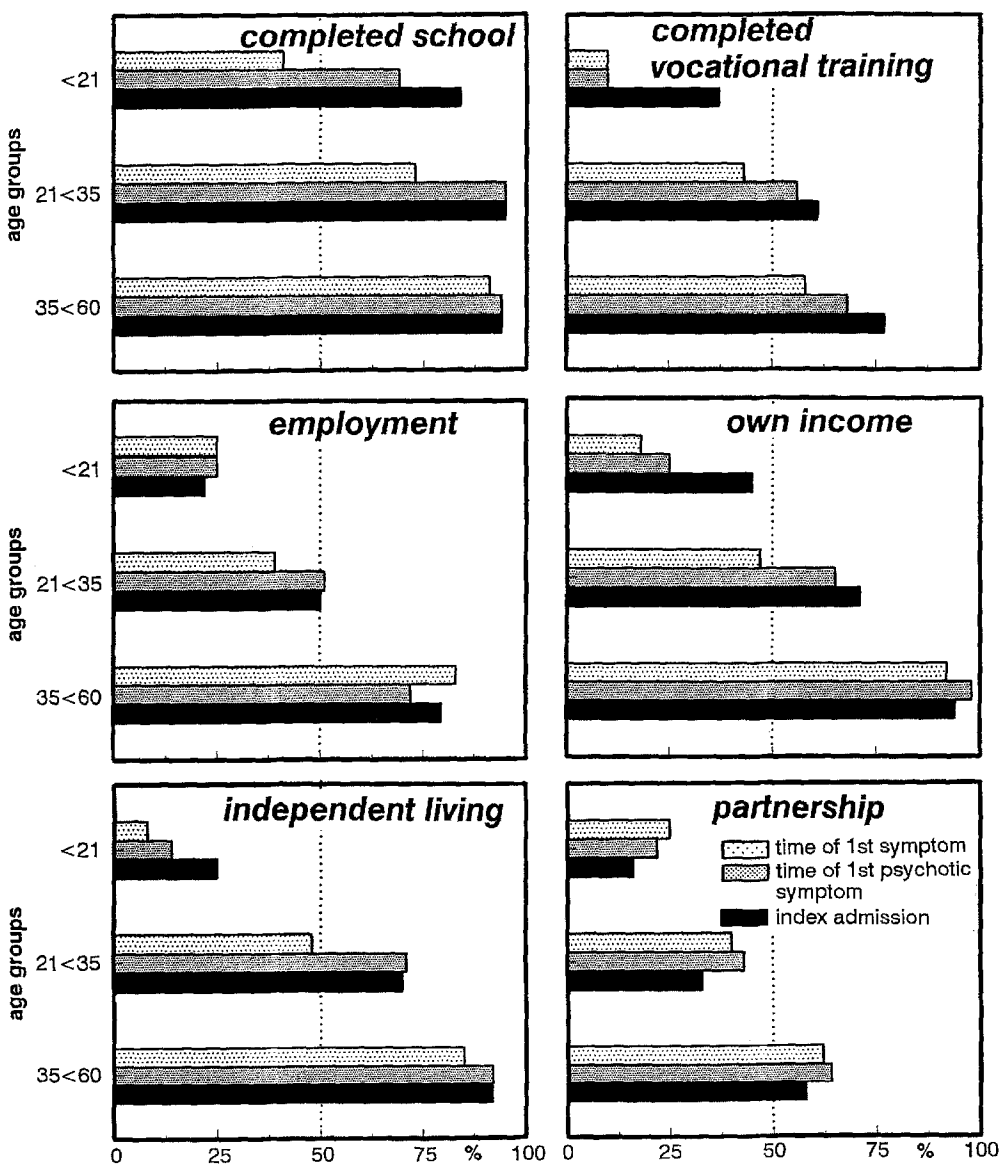


Fig. 6 Social development in prephases and early phases of schizophrenia. Age groups according to first psychotic symptom

the only exception of completed school – at all the time points of the hidden early course of schizophrenia: at the beginning and at the end of the prodromal phase and at first admission.

Normal social development, however, defined as the acquiring of new social roles, continues to a substantial degree during the prodromal phase, but less during the shorter pre-psychotic phase. The percentage of patients in the youngest group who finished school education rose from 41% at the first sign of the disorder to 84% at index admission. Also, many patients who completed their school education and occupational training left their parental home for independent accommodation, despite the accumulating symptomatology during the prephase of the illness. Nevertheless, as expected, the youngest group showed the highest percentage of patients with further disruptions in their social biography in the prephase prior to first admission. Of the children and adolescents 33% quit school during the prephase, due to abnormal behaviour or difficulties in keeping up with academic standards, whereas 20% were forced to give up their vocational training. Even after finishing school education some of the early-onset patients failed to get a job, and thus their own income, once the disorder had broken out. On the other hand, there were some patients, even in the medium- and late-onset group, who managed to achieve limited social ascent by finishing vocational training in the prephase of the psychosis.

The patients' socio-economic backgrounds, as compared to the father's occupation, did not show any significant differences between the three age groups. The pronounced differences between the three age groups in the social conditions at the beginning of schizophrenia were mainly accounted for by differences in the levels of social development at onset and not for being born into a more disadvantageous social environment. The differences observed at first admission in the social-status components attained between the age groups resulted mainly from the disruptive impact of the disorder on social development in the prodromal and the psychotic prephases.

Social disability

In a further analysis we tested whether besides the objective social situation, i.e. the achieved level of social development at illness onset, a subjective measure of social functioning (i.e. social disability), differed in early- and late-onset schizophrenia. The assessment of social disability was conducted by means of an interview with a key person closest to the patient. By using the Disability Assessment Schedule (DAS-M; WHO 1988; German version: Jung et al. 1989) we were able to estimate how well the patient's social functioning was adapted to the expectations and demands of his or her social environment.

Figure 7 shows that the youngest age group had the highest disability score at first admission. Because the instrument cannot be administered retrospectively, we were unable to obtain disability scores for the prephase. However, in the representative subsample for 133 first-episode cases mentioned at the outset, DAS interviews were conducted at four waves from index admission until 3 years thereafter. Again, the three age groups, defined by age at the first sign of the disorder and, secondly, at the first psychotic symptom, were compared. We found that the disadvantage of the youngest group persisting at the beginning had diminished almost to zero as early as 6 months after index admission. Higher disability scores for males compared with females at first admission and thereafter were observed in all age groups. They seemed to increase with age. But again, due to the lack of statistical power, the age groups could not be subdivided further by gender to obtain valid results.

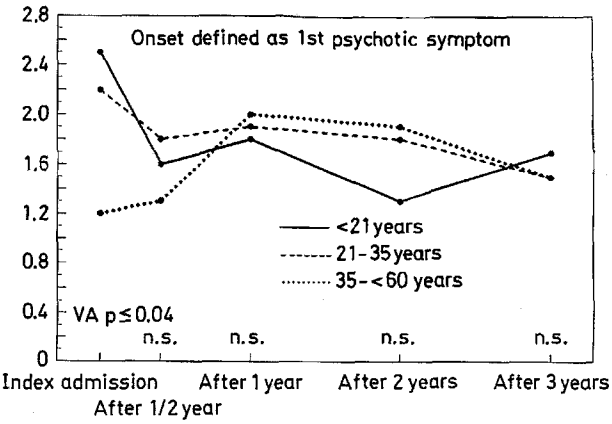


Fig. 7 Course of total assessment of social disability (mean values)

In neither group did the mean disability score increase in the period of 6 months (i.e. after remission of the first episode) to 3 years after first admission. Obviously, in contrast to objective social-status deficits, psychological processes of adaptation do not seem to deteriorate, at least as judged by group means; instead; they seem to contribute to a more effective coping with objective social disadvantage in a certain proportion of cases. But this might also be due to lower demands in the patients' environment.

Further symptom-related course of schizophrenia from first admission until 3 years after

For both definitions of onset the mean values of the CATEGO syndrome scores in the course following first admission did not clearly differ between the age groups (Manova). The total scores equalised after the second measurement, i.e. 6 months after first admission. The number of symptoms clearly decreased for all groups, probably due to the remission of the first psychotic episode. There was only one interaction between group and time, and no group effects (Fig. 8). The interaction is possibly due to to the very small number of patients in the late-onset group which shows large variance of scores. The course of the negative symptomatology, was similar

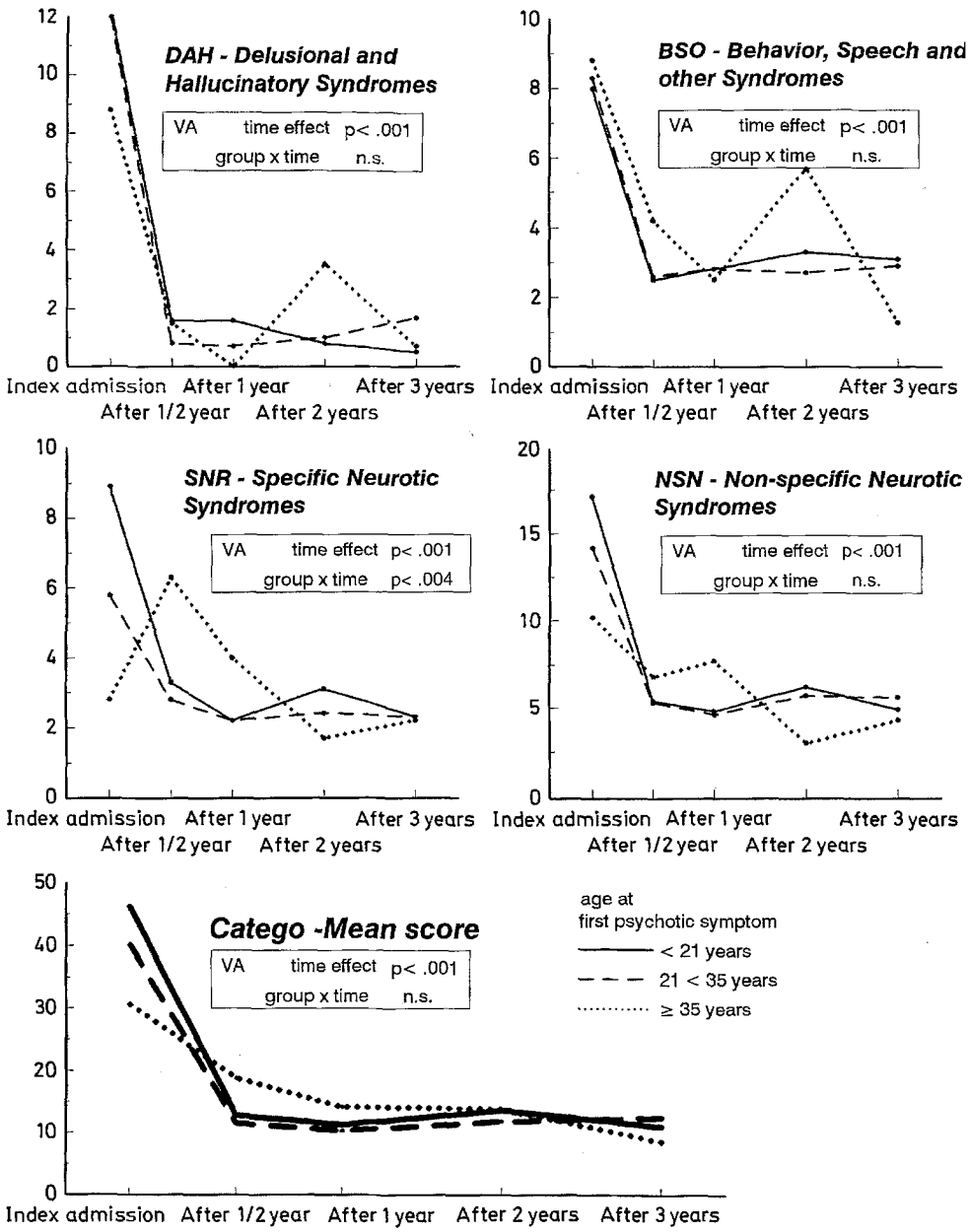


Fig. 8 Symptomatology during course of illness

in all groups as well. In accordance with earlier studies, no differences were found in the symptom-related course of early-onset, medium- and late-onset schizophrenia. The total mean score of the SANS reached its maximum at index admission, decreased sharply during the following 6 months, and then remained stable. The changes in course were clearly smaller than for the positive symptomatology. Also, the number of readmissions did not significantly differ between the age groups during the 3-year risk period.

Conclusions

First admissions with a precise diagnosis of schizophrenia hardly occur before age 12 years, but the disorder often begins long before first admission. In three-quarters of all cases the first psychotic episode is preceded by a prodromal phase of about 5 years. When age at the first sign of the disorder, i.e. at the beginning of the prodromal phase, is taken as a basis, the share of early-onset schizophrenias (<21 years) in the total schizophrenia incidence until age 60 years rises to 47%, and the share of schizophrenias starting before age 10 years to 4%. If onset is defined by age at the first positive symptom, i.e. at the beginning of the psychotic episode, 21% of the schizophrenias start before age 21 years.

Boys more often than girls develop schizophrenia before reaching adulthood (<21 years). However, the most pronounced gender difference in incidence occurs only after age 30 years with a clear predominance of female onsets.

The symptomatology of early-onset psychosis is characterized by the predominance of undifferentiated psychotic symptoms and frequent signs of emotional and conduct disorders, reflecting incomplete cognitive and personality development – and underlying incomplete brain maturation – on the one hand, and differences in the response patterns of boys and girls in this age range on the other. The initial course of early-onset schizophrenia hardly differs from medium- and late-onset schizophrenia, except for a slightly longer prodromal phase. The onset of schizophrenia at an early stage of social development disrupts further social ascent, a finding more pronounced in boys, due to their lower mean age of onset compared with girls.

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