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Is schizophrenia a disorder of all ages? A comparison of first episodes and early course across the life-cycle

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ABSTRACT

Background. The heterogeneity of schizophrenic and delusional syndromes by age of onset has frequently been discussed.

Methods. The age distribution of symptoms and 5 year course was studied in a population-based first-episode sample admitted to 10 psychiatric hospitals before the age of 60 ($N = 232$) and in a clinical sample without age limit of consecutive first admissions to a single hospital ($N = 1109$), both samples with broadly diagnosed schizophrenia.

Results. Early-onset patients, particularly men, presented more non-specific symptoms and higher PSE-CATEGO total scores than late-onset patients. In men, symptom severity decreased with increasing age of onset. In women, it remained stable except for an increase of negative symptoms with late-onset. Only a few symptoms changed markedly with age: disorganization decreased, while paranoid and systematic delusions increased steeply across the whole age of onset range. Pronounced age- and sex-differences emerged in illness behaviour, socially negative behaviour and substance abuse. Within the group of late-onset psychoses there were continuous transitions in symptom profiles and no discrimination between schizophrenia and paranoid psychosis or late paraphrenia. The main determinant of social course was onset level of social development. Early-onset patients did not improve in social status, while late-onset patients, prior to retirement, suffered considerable decline in social status.

Conclusions. Gender differences in age at onset and in age trends in symptom severity support the hypothesis of a mild protective effect of oestrogen. Social course results from an interplay between biological factors (age at onset and functional impairment) and development factors (level of social development at onset and illness behaviour).

INTRODUCTION

In 1896, Kraepelin described dementia praecox as a disorder of adolescence and early adulthood. In 1911, Eugen Bleuler reported on illnesses manifesting themselves with similar symptoms after the age 40, which his son Manfred (1943) termed 'late-onset schizophrenias'. There are, however, ongoing controversies whether early- and late-onset schizophrenias are different, or similar, disorders, and which delusional disorders of the elderly should be grouped with late-onset schizophrenias, and which of them should be classified separately, for example, as late paraphrenias, paranoid psychoses or merely as delusional syndromes (Roth & Morrissey, 1952; Fish, 1960; Grahame, 1984; Holden, 1987; Almeida *et al*. 1994). Goldstein *et al*. (1990) and

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Castle & Murray (1991) argued that schizophrenias in late adulthood and old age, in elderly women in particular, are affective diseases merely presenting schizophrenic symptoms. Behind the question of a valid diagnostic classification lies the issue of the underlying aetiology.

For a better understanding of the uniformity *versus* diversity of schizophrenic psychoses at different ages comparisons not only within and between particular age groups, but also across the life cycle are needed (Russell, 1994). By this approach possible 'points of rarity' can be identified, which provide empirical criteria to distinguish age-related subtypes. To avoid distortions that might arise from different stages of illness or from age-related differences in environmental factors after a lengthy course of illness the comparisons should be based on first-episode data or – as a second best alternative – on first-admission data.

This paper reviews some previous data on the morbid risk for functional non-affective psychoses across the life cycle and presents new results on their clinical manifestation from adolescence to old age.

Morbidity risk across the life cycle

It is well established that the morbid risk for schizophrenia changes with age and that gender has a strong influence on age at onset: based on the first sign of the disorder, incidence rates in men are at their highest in young adults, whereas in women they increase later with a broader peak extending beyond the age of 30 and a second (lower) peak between ages 45 and 49. Fig. 1 demonstrates these converging results from the representative population-based ABC (Age, Beginning, Course) first-episode sample ($N = 232$) (Häfner *et al.* 1993) and the national Danish psychiatric case register (Riecher-Rössler *et al.* 1998). These findings corroborate those of the WHO Determinants of Outcome Study (Jablensky *et al.* 1992) and the Camberwell case-register (Castle *et al.* 1995). The second peak for women results in a female predominance in these age groups, for instance, an odds ratio of 2·16 ($P < 0{\cdot}05$) for patients with the first psychotic symptom between the ages of 36 and 59 (Häfner *et al.* 1993). The second peak coincides fairly well with the average age for menopause, thus supporting the hypothesis that oestrogen may have a protective effect (Lewine, 1980; Seeman, 1982; Seeman & Lang, 1990) in delaying the onset of schizophrenia in women (Häfner *et al.* 1992*a*).

The influence of senescence on the morbid risk for schizophrenia is controversial: Harris & Jeste's (1988) review as well as national Danish case register data (Häfner *et al.* 1989) show a clear decrease after the age of 60 in first-admission rates based on a clinical diagnosis of schizophrenia. In contrast, applying a more restrictive DSM-III-R diagnosis of schizophrenia, Castle & Murray (1993), who rated Camberwell case-register files from 1965 to 1984, found a considerable increase in old age, particularly in women. On the basis of first admissions with a clinical diagnosis of schizophrenia to other British and Dutch case-registers van Os *et al.* (1995) reported increases in admission rates by 90% to 150% between the seventh and the tenth decade of life. These different results can be attributed, in part, to methodological variations between the studies (e.g. diagnostic criteria, validity of case-register diagnoses), but they also reflect the many difficulties in case-finding, particularly in old age (Post, 1966; Perrson, 1980; Krauss, 1989). Population studies suggest that the proportion of the treated to true incidence of schizophrenic and paranoid syndromes decreases with age. While the treated incidence of schizophrenia until the age of 60 approximates to 100% of the true incidence – at least in regions with full health insurance and easily accessible services like Southern Germany (Weyerer & Dilling, 1984) – a considerable proportion of the elderly population tends to refuse to seek treatment, or even to participate in diagnostic assessments, because of suspiciousness partly attributable to paranoid syndromes. The hidden prevalence of paranoid syndromes in the elderly can be estimated roughly from two recent German community studies (Cooper & Sosna, 1984; Baltes *et al.* 1993); while the point prevalence rate of definite cases of all types of delusional disorders in the elderly was about 1%, the proportions of persons refusing because of suspicious/paranoid tendencies were considerably higher (7% and 10%). Therefore, depending on their methodology, population studies, also, produce too small and presumably distorted proportions of the true delusional or paranoid morbidity in old age.

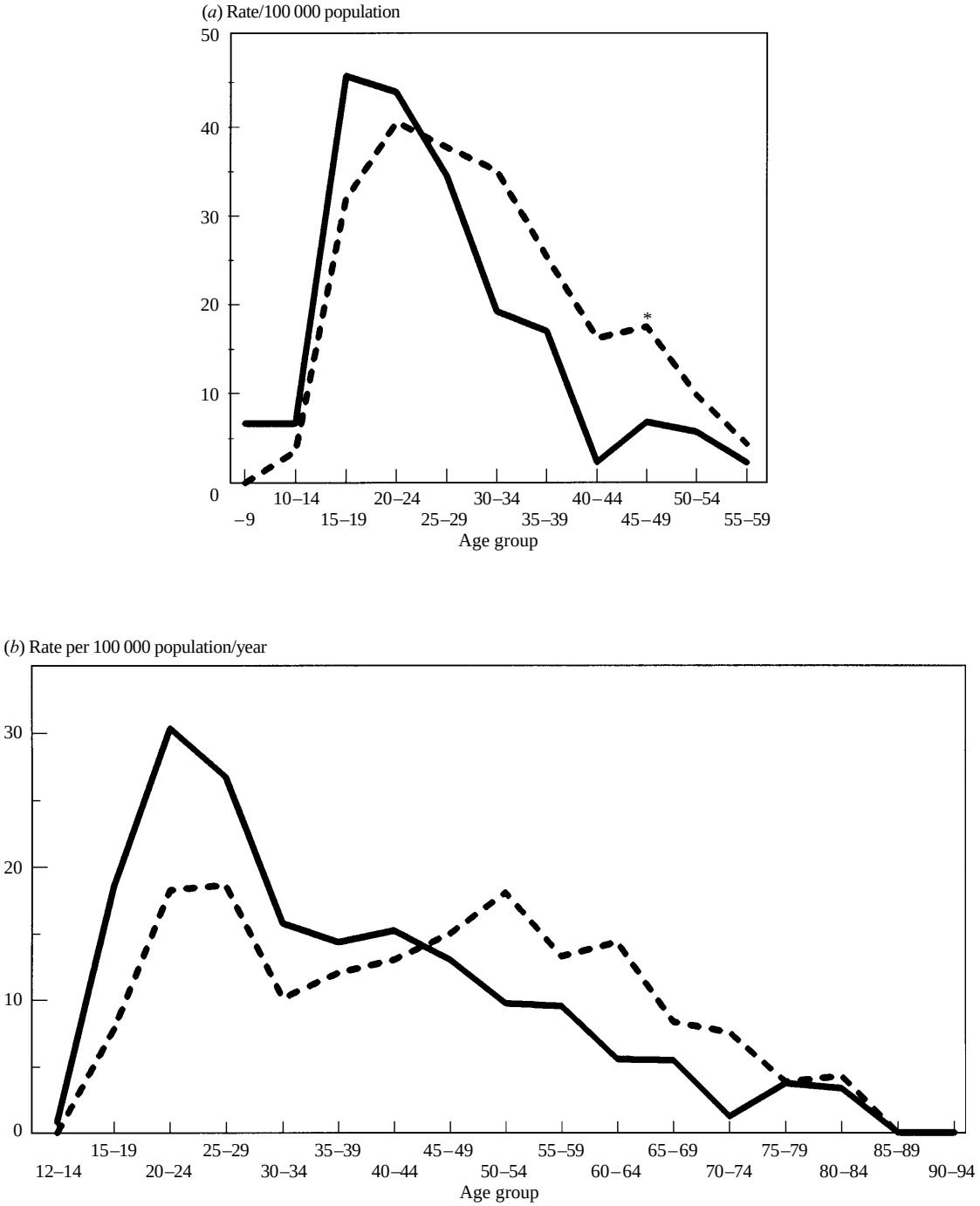

FIG. 1. (*a*) Distribution of age at onset of schizophrenia (first psychotic symptom) by sex (——, males, $N = 117$; – – –, females, $N = 131$), ICD-9: 295, 297, 298.3 and 298.4. ABC Schizophrenia Study – $N_{\text{population}}$ = approximately 1·5 million, $N_{\text{first-episode sample}} = 232$; $^{*}P < 0{\cdot}05$. (*b*) Population-based first-admission rates for schizophrenia in Denmark, 1976, ICD-8: 295 (——, males, $N = 329$; – – –, females, $N = 250$).

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Clinical presentation across the life cycle

Severity of symptoms

The vulnerability–stress model of schizophrenia (Zubin & Spring, 1977) implies that individuals with a high disposition fall ill earlier in life, whereas those with a lower grade of vulnerability fall ill later. It seems plausible to assume that a high disposition coincides with a more severe clinical presentation of the disorder. Therefore, increasing age of onset should correlate with milder symptomatology. An interaction of age with gender in symptom severity can be expected from the assumed mild protective effect of oestrogen against psychotic symptoms. Evidence in support of this hypothesis emerged from animal experiments, receptor binding studies (Häfner *et al.* 1991) and a controlled clinical study (Riecher-Rössler *et al.* 1994). Oestrogen was found to modulate various neurotransmitter systems (Seeman & Lang, 1990), for instance, the sensitivity of central D_2 receptors, and to correlate inversely with schizophrenic symptomatology (Häfner *et al.* 1992*a*, 1993, 1995). Oestrogen treatment of neonatal rats (Häfner *et al.* 1991) demonstrated a structural effect on dopaminergic neurotransmission.

On the basis of these results it could be speculated that oestrogens might modulate both the age distribution of onset and symptom severity in women, but not in men: without the protective effect of oestrogens men should show a high incidence at a young age, which decreases over time, whereas in women oestrogens should delay the onset of schizophrenia at least in some individuals, thus resulting in slightly lower incidence rates in young age groups and an excess of new cases shortly before and around menopause when the oestrogen effect vanishes. With regard to symptom severity one may predict that without a protective effect men should develop the most severe forms early in life and less severe forms later in life. Due to the protective effect of oestrogen women should present slightly milder early-onset schizophrenias than men, but around and shortly after menopause more severe forms of late-onset schizophrenias would be expected. The best way of testing these hypotheses is to compare the frequency and severity of first psychotic episodes by age in a population-based sample. In our study the ABC sample was suitable for this purpose.

Type of symptoms

Several studies (Pearlson *et al.* 1989; Howard *et al.* 1993; Yassa & Suranyi-Cadotte, 1993; Jeste *et al.* 1995) have attempted to dichotomize schizophrenic patients according to the onset of first psychotic symptoms before *versus* after age 45. A repeated finding was a higher frequency of persecutory delusions in the late-onset cases and less prominent other psychopathological differences between the age groups. Häfner *et al.* (1993) compared three age groups in a large population-based first-admission sample. While the nuclear symptomatology of schizophrenia did not differ significantly between the age groups, some age effects on additional symptoms were found: anxiety syndromes and substance abuse peaked in patients under the age of 25, depressive symptoms in patients aged 25 to 34, and persecutory delusions were most frequent in patients aged 35 to 59. The only items that showed significant confounding with sex were 'anhedonia', which reached a maximum in late-onset women, and 'distorted relationship with friends and peers', which predominated in young males.

Post (1966) emphasized the heterogeneity of delusional and schizophrenic disorders with onset after the age of 60. Indeed, a variety of diagnoses are assigned to these conditions, but several studies (Harris & Jeste, 1988; Pearlson *et al.* 1989; Mayer *et al.* 1993) have found no marked differences in symptomatology between cases diagnosed with late-onset schizophrenia and those with other delusional disorders, for example, late paraphrenia. Only bizarre or 'fantastic' delusions have repeatedly been found to be more frequent in late-onset schizophrenia than in other diagnostic groups (Harris *et al.* 1988; Howard *et al.* 1993; Yassa & Suranyi-Cadotte, 1993). These results foster the conclusion that delusional symptoms become more frequent with later age of onset, whereas other schizophrenic symptoms remain equally frequent, or decrease, because of a lower severity. Most of these studies, however, relied on retrospective assessments, samples of small size, or including first-admissions as well as chronic cases. Therefore, the hypotheses need to be

tested prospectively in large enough samples and on cases with identical stages of illness, ideally the first psychotic episode. Since our population-based first-episode sample was limited to age < 60 years, we had to study the distribution of schizophrenic symptoms across the whole age range in a clinical first-admission sample. For this reason, these results need more additional validation than those on the hypotheses tested in the first-episode sample.

Consequences of age-dependent social conditions at illness onset

Age presumably influences not only symptomatology, but also social course and outcome. And age at onset presumably interferes with the patients' social development, particularly if the main age of risk falls in the period of life characterized by the steepest social ascent. The disorder intrudes into the social biographies of young and old patients at very different levels of social development. Onset during adolescence implies that many social roles (graduating from school, completion of vocational training, job and financial autonomy, leaving the parents' home, establishing a partnership) have not been accomplished yet. When the onset of schizophrenia happens during the fourth decade of life or later, the patients have already completed most of these social tasks. If the disorder impairs further social ascent by producing cognitive deficits and social disability, the level of social development at the beginning of the disorder must exert some influence on the further social course. Early-onset patients can be expected to be impaired in fulfilling these roles from the beginning (they are 'non-starters' according to Dunham (1965)), whereas late-onset patients should suffer some decline from an already achieved social status (i.e. social drift) or show stability regarding those roles that (once achieved) are usually not lost (e.g. independent living, tenure, marriage). The stage of social development at onset can thus be expected to determine social outcome.

Clinical and social course

Kay & Roth (1961) felt that over time, especially in chronic courses, the clinical picture of early- and late-onset schizophrenia becomes indistinguishable. The vulnerability–stress concept of schizophrenia, as considered above, yields another hypothesis: early-onset should be associated with more severity (at least in men) and therefore with a worse outcome. Later age of onset should yield a better symptom-related outcome, for instance, less schizophrenic symptoms.

Hypotheses

On the basis of the literature cited and the results of our previous studies we formulated hypotheses on the influence of age: (1) on the severity of the disorder and on symptoms in the first episode in men and women; (2) on the symptom-related course; and, (3) on the social course until 5 years after first admission.

The hypotheses were in detail as follows.

1.1 Sex not taken into account, an increasing age at onset should correlate with milder symptoms (in the first episode).

1.2 An interaction with sex in symptom severity can be expected from the assumed mildly protective effect of oestrogen: compared with men early-onset women should show a slightly lower incidence and severity and late-onset women a clearly higher incidence and greater severity of schizophrenia.

1.3 In the first episode the core symptoms of schizophrenia, closely related to the disorder, and their type should vary only little across the whole age of onset range, whereas single developmental symptoms (disorganizational symptoms, systematic delusions) should strongly correlate with age.

1.4 Schizophrenia and delusional disorders of old age (> 60) should be impossible to distinguish empirically by their symptoms in the first episode.

2. The group means of the symptom-related course from onset until 5 years after first admission should vary only little with age and sex.

3. Age at onset should have an indirect influence on the social course of schizophrenia.

3.1 The level of social development at onset should influence medium-term social course and outcome.

3.2 Age-dependent, and sex-specific, illness behaviour should influence social adjustment and medium-term social course and outcome.

To test these hypotheses two samples were

studied. To perform age comparisons or age group-related analyses the samples were divided into subsamples with defined age ranges.

METHOD

ABC study sample

From the first sample a population-based subsample of 232 first-episode cases were recruited. This population-based subsample from the ABC Schizophrenia Study comprised 84% of 276 consecutive first admissions in the age range of 12 to 59 years with a broad diagnosis of schizophrenia (ICD-9: 295, 297, 298.3/4) to 10 mental hospitals or units in a 2-year period (1987–1989) from a population of 1·5 million in Germany. None of the patients had had a psychotic episode before. Symptomatology, functional impairment and social disability were assessed by clinically experienced, trained interviewers (psychiatrists and psychologists) by using the Present Stage Examination – PSE (Wing *et al*. 1974), the Scale for the Assessment of Negative Symptoms – SANS (Andreasen, 1983), the Psychological Impairments Rating Schedule – PIRS (Biehl *et al*. 1989) and the Disability Assessment Schedule – DAS (World Health Organization, 1988; Jung et al. 1989). The sample and the instruments have been described in detail elsewhere (Häfner *et al*. 1993).

Onset and course before first admission were assessed retrospectively with the standardized 'Interview for the Retrospective Assessment on the Onset of Schizophrenia', IRAOS (Häfner *et al*. 1992*b*; Maurer & Häfner, 1995). This instrument includes a large section on the patients' social biography.

The ensuing course of the symptoms and social consequences of schizophrenia were prospectively followed up in a population-based subsample of 115 first-episode cases from the ABC study sample at five cross sections over 5 years (first admission, 1/2, 1, 2, 3 and 5 years later). In each case the history of the disorder was assessed from onset until first admission and so a complete picture of the course of schizophrenia was obtained, extending from the first sign to the first negative and first positive symptom and until the climax of the first episode, first admission and 5 years later.

CIMH (Central Institute of Mental Health) first-admission sample

This series included all 1109 patients (without age limitation) who were for the first time admitted to the CIMH with a broad clinical diagnosis of schizophrenia (ICD-9: 295, 297, 298.3/4) from 1978 to 1992.[1] The catchment area of the CIMH Psychiatric Department is the German city of Mannheim with a population of 330000, but about 40% of the admissions come from the adjacent areas. In this respect this sample was not strictly population-based. Each patient was assessed shortly after hospitalization by a psychiatrist using the systematic AMDP symptom check list ('Arbeitsgemeinschaft für Methodik und Dokumentation in der Psychiatrie', AMDP 1981), the main items of which are identical with the PSE. The 140 individual items of this symptom check list as well as their aggregation, eight empirically derived syndromes (Gebhardt *et al*. 1983), were analysed.

Statistical procedures

To test the significance of associations between variables that are dichotomous (gender) and/or have a limited number of numeric values (age group) the χ^2 test was used. Fisher's exact test was computed additionally when there were fewer than 20 cases in fourfold tables. Student's *t* statistics for independent samples were calculated to test the two-tailed significance in comparing sample means. To determine the influence of different independent variables on the assignment of patients to a diagnosis of schizophrenia or paranoid psychosis the stepwise logistic regression was used. With this procedure the effect of dichotomous or numerical variables on a dichotomous dependent variable can be estimated. Computed beta coefficients, ranging from -1 to $+1$, showed the significant effect of some variables on the dependent variables and also gave the explained variance. The increase or decrease in symptoms with age was tested with linear logit models. Here age was used for predicting a dichotomous dependent variable (symptom yes *v*. no). The model of a linear

[1] The authors gratefully acknowledge the support of Dr W. Häfner-Ranabauer, Director of the CIMH Unit 'Scientific Documentation', for providing the data base.

Table 1. *Symptomatology at first admission: CATEGO syndrome scores and total score by three age groups* (N = 232)

Age at onset*	12–20	21–35	36–59	ANOVA *P*
DAH	11·2	10·3	10·1	< 0·7
BSO	8·7	7·8	7·4	< 0·04
SNR	9·6	6·7	6·6	< 0·003
NSN	16·3	15·5	13·3	< 0·08
Total score	45·9	40·4	37·7	< 0·03

* Defined by first psychotic symptom.

DAH, delusional and hallucinatory syndrome; BSO, behaviour, speech and other syndromes; SNR, specific neurotic syndromes; NSN, non-specific syndromes.

increase or decrease in symptoms over the age groups was tested with the 'goodness of fit' measure and significant β-coefficients of the independent variables (Haberman, 1982). To determine subgroups of patients empirically the Grade of Membership Model – GOM (Woodbury & Manton, 1989) was applied. Contrary to traditional methods of subtyping, such as cluster analysis or latent class analysis, this method assigns patients to more than one clinically relevant subgroup called pure types. Based on categorical data and maximum likelihood principals GOM first determined the number of pure types characterized by a specific symptom profile. Then the association between pure types and single symptoms was determined and measured by the pure types probabilities and the association between patients and respective pure types of GOM-scores. Both parameters were estimated simultaneously.

RESULTS

Severity of symptoms

Severity was determined by three indicators: type of onset (acute/subacute/chronic), symptom-related course up to first admission and symptom scores in the first psychotic episode.

The proportions of types of onset did not differ significantly between the three age groups with percentages ranging between 14 and 26% for acute onsets ($\leqslant 4$ weeks), between 10 and 26% for the subacute onsets (> 4 weeks $\leqslant 1$ year) and between 52 and 71% for the chronic type of onset (over 1 year). The accumulation of positive, negative and non-specific symptoms until the climax of the first episode, as based on the mean sum scores of the IRAOS items, also showed strikingly similar patterns for the three age groups (Häfner *et al*. 1993). PSE/CATEGO symptom scores at index admission showed a small, but steady decrease with increasing age of onset. The mean total score fell from 46 in the youngest group to 38 in the oldest (Table 1). The CATEGO subscores DAH (delusions and hallucinations) and BSO (behaviour, speech and other syndromes) contributed quantitatively only slightly to the significant age effect, which was primarily brought about by lower scores on the non-schizophrenia-specific syndromes NSN (non-specific neurotic syndromes) and SNR (specific neurotic syndromes) in the older groups.

A gender comparison of symptom measures in two extreme age groups with early *v*. late onset (i.e. first psychotic symptom before age 21 *v*. after age 40) revealed different age trends for men and women, as hypothesized (Table 2). On all symptom dimensions late-onset men scored lower than early-onset men reached a level of significance of 0·05 or below. In contrast, for late-onset women not a single indicator was significantly more favourable and one, the SANS global score, was more unfavourable than in the early-onset group. Consequently, the milder symptomatology in late-onset schizophrenia was accounted for by men alone.

Type of symptoms

In the CIMH first-admission sample of 1109 cases with a broad diagnosis of schizophrenia and no age limit the mean scores on the paranoid–hallucinatory, depressive, hostility and apathy AMDP syndrome did not differ significantly between the 5-year age groups with the exception of the neurological (χ^2: $P < 0{\cdot}001$) and the psycho-organic syndrome (χ^2: $P < 0{\cdot}02$), both showing the highest scores after age 64 years. On the level of individual symptoms, frequencies, particularly of negative symptoms, showed little variation with age except for the pronounced age trends illustrated in Fig. 2, based on 5-year age groups from 15 to 19 years until 75 years and over (the numbers at higher ages were too small). The percentages of cases presenting 'systematic delusions' and 'paranoid delusions' increased linearly with age across the total age of onset range, e.g. 'systematic de-

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Table 2. *Sex differences in symptom scores at time of first psychotic episode – early* versus *late onset*†

	Men			Women		
Symptomatology	Early $N = 28$	*v.* Wilcoxon	Late $N = 9$	Early $N = 21$	*v.* Wilcoxon	Late $N = 24$
DAH	12·1	0·02*	↓5·7	10·0	0·95	10·5
BSO	8·6	0·29	7·3	8·9	0·44	7·9
SNR	10·7	0·11	7·3	8·2	0·42	7·1
NSN	18·9	0·03*	↓11·4	13·0	0·58	13·8
Total score	50·3	0·02*	↓31·8	40·0	0·80	39·2
SANS	9·3	0·29	6·6	6·7	0·08⁺	↑9·5
PIRS	10·7	0·26	8·4	9·8	0·73	10·5
DAS-M	3·0	0·06⁺	↓1·8	1·9	0·61	1·8

† Age at first psychotic symptom < 21 years *v.* $\geqslant 40$ years.
⁺ $P < 0{\cdot}1$; * $P < 0{\cdot}05$.
Arrow marks the direction of age difference.

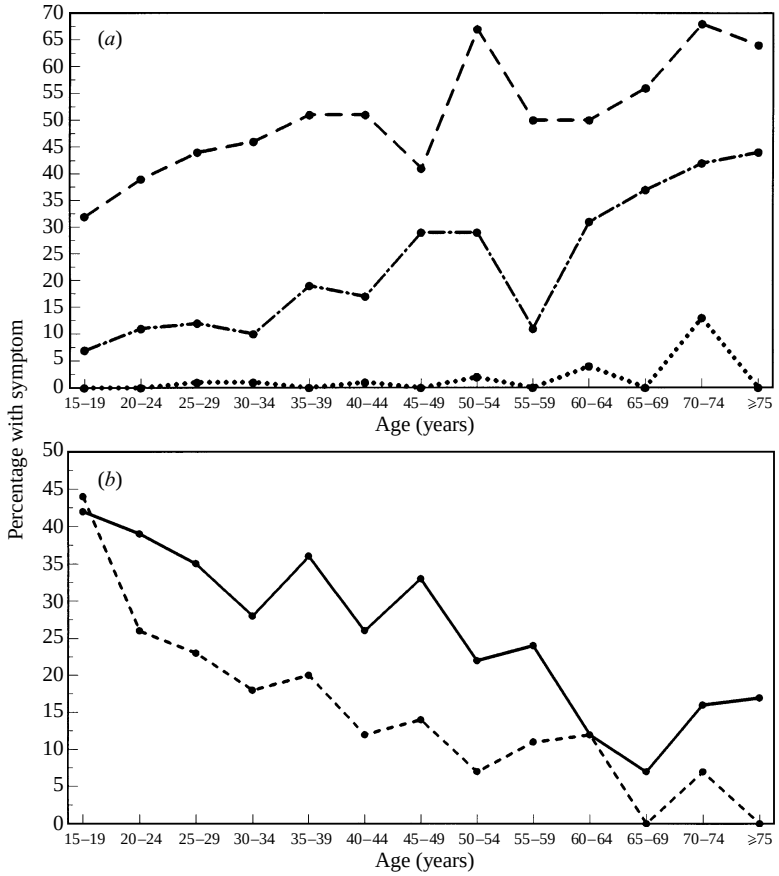

FIG. 2. Psychotic symptoms with significant age trends – CIMH administrative data, $N = 1109$. (*a*) Percentage with symptom: ·–·, systematic delusions; ———, paranoid delusions; ·····, delusion of poverty. (*b*) Percentage with symptom: ——, incoherence of thought; – – –, disordered sense of self. $\chi^2 = P < 0{\cdot}001$.

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lusions' increased linearly with age across the total age of onset range, e.g. 'systematic delusions' sixfold. The opposite was found for symptoms like 'incoherence of thought' and 'disordered sense of self', whose prevalences decreased almost steadily over the age range. For the depicted symptoms, goodness-of-fit tests demonstrated highly significant linear increases (decreases) of frequency in logit with age.

In the very late-onset group (i.e. after age 60) patients with a clinical diagnosis of schizophrenia (ICD 295) and patients assigned to a diagnosis of paranoid disorder (ICD 298.3/4) did not differ distinctly in their symptom profiles (Table 3). The two groups showed significant differences in the frequency of only 18 (13%) out of 140 psychopathological items. The most pronounced finding was that all the 18 symptoms showing age differences were more prevalent in patients with a diagnosis of schizophrenia, thus demonstrating a difference in quantity, but not in the profiles. First-rank symptoms were also present in patients with a diagnosis of paranoid disorder or paraphrenia.

The stepwise logistic regression was applied to obtain more detailed information on the criteria by which the CIMH clinicians assign elderly patients to a clinical diagnosis of schizophrenia *versus* paranoid psychosis. To ensure statistical power a large subsample of the total first-admission sample was investigated, namely all 352 first admissions at age 40 and over. Age was found to be the only variable essentially contributing to the diagnostic decision (paranoid disorder *versus* schizophrenia) with a beta coefficient of 0·71 ($P \leqslant 0{\cdot}001$) and explaining 22% of the variance.

The attempt to discriminate precisely between defined subgroups in the late- and very late-onset group by the grade of membership model (Woodbury & Manton, 1989) failed. In this subsample, on which the logistic regression, too, was performed, Riecher-Rössler *et al.* (1997) identified six 'pure types': (1) paranoid–hallucinatory symptoms; (2) few specific symptoms and a preponderance of non-specific symptoms; (3) schizoaffective, manic type; (4) primarily negative symptoms/residual syndrome; (5) delusions of reference and persecution/paranoid psychosis; (6) paranoid–hallucinatory syndrome with systematized delusions/paranoid schizophrenia. Mean age of onset by these types showed a minimum of 38 years in type 1 and a maximum of 55 years in type 5. The mean age of patients assigned to type 6 was 54 years. These higher mean ages of patients with paranoid delusions (type 5 and 6) and systematized delusions (type 6) indicate that these symptoms become more frequent with increasing age. By compiling a matrix of associations Riecher-Rössler *et al.* (1997) demonstrated considerable overlap between the six pure types.

Consequences of age-dependent social conditions at illness onset

Fig. 3 shows the percentages of patients in the three age groups fulfilling key social roles at the emergence of the first sign of mental disorder. Significant differences are observable.

Table 3. *Comparison of patients aged* > 60 *years with a diagnosis of schizophrenia* (N = 29) v. *paranoid psychosis* (N = 85)†

Items from the AMDP symptom check list (total no. of items 140) with significant differences‡ between the diagnostic groups	Schizophrenia %	Paranoid psychosis %	*P*
Tangentiality of speech	31·0	8·2	**
Incoherence of thought	27·6	9·4	*
Bodily hallucinations	34·5	14·1	*
Disorders of self	13·8	1·2	**
Thought withdrawal	10·3	1·2	*
Thought intrusion	13·8	2·4	*
Other delusions of influence	27·6	9·4	*
Elated mood	13·8	3·5	*
Restlessness	44·8	23·5	*
Exaggerated self-esteem	6·9	0	*
Lack of drive	13·8	3·5	*
Stuporous	6·9	0	*
Increased motor activity	27·6	9·4	*
Symptoms better in the evening	17·2	3·5	*
Aggressiveness	17·2	4·7	*
Needs help in hygiene	17·2	4·7	*
Waking at night	72·4	44·7	*
Obstipation	20·7	7·1	*

* $P < 0{\cdot}05$; ** $P < 0{\cdot}01$.

† CIMH administrative data, clinical diagnosis ICD-9 295 *v.* 297, 298.3.4.

‡ A procedure of correcting for multiple testing (e.g. Bonferroni correction) was not applied. In a total of 140 comparisons of single items none of the differences would have attained significance. The tests of significance were used for defining a threshold. The differences in all those items fulfilling this criterion proved to be quantitatively large, as expected, and pointed into the same direction. This clear trend of difference between schizophrenia and paranoid psychosis would no longer have been visible after correction for multiple testing at a single item level.

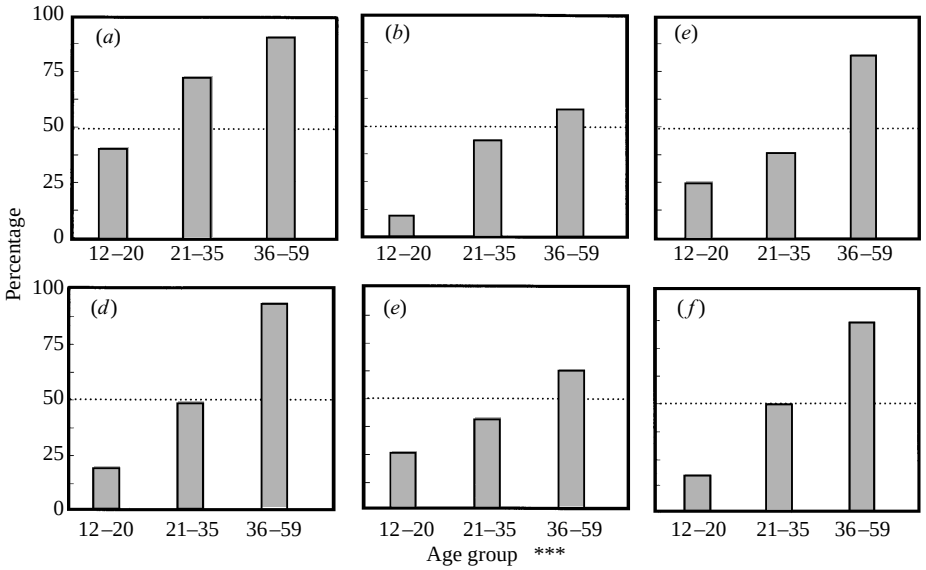

FIG. 3. Level of social development by six key roles at the onset of schizophrenia (= first sign of mental disorder). (*a*) Finished school education; (*b*) Finished occupational training; (*c*) Employment; (*d*) Own income; (*e*) Partnership; (*f*) Own accommodation. *** Group differences $P < 0{\cdot}001$ (χ^2).

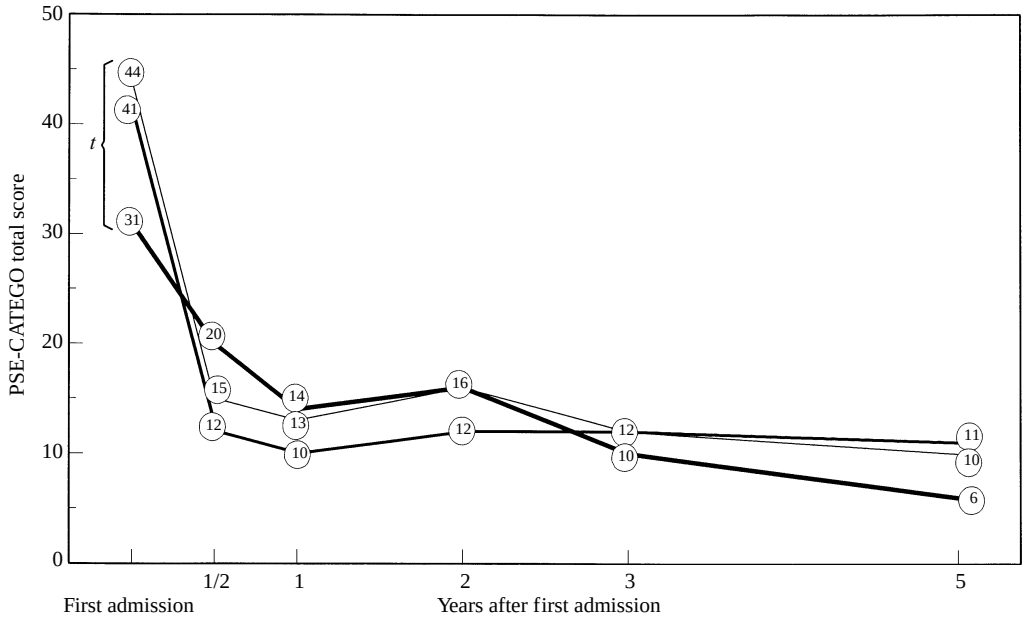

FIG. 4. Symptom-related course (PSE-CATEGO total score) over 5 years after first admission – ABC follow-up sample, $N = 115$ – ICD-9: 295, 297, 289.3, 298.4. (Age at first admission: ——, 12–20 years; ▬, 21–35 years; ▬, 36–59 years; t = statistical trend in ANOVA.)

Clinical and social course

The significant differences between the three age groups in some symptom scores in the acute episode were no longer present at the 6-month follow-up or later until 5 years after first admission. The same was true for social disability

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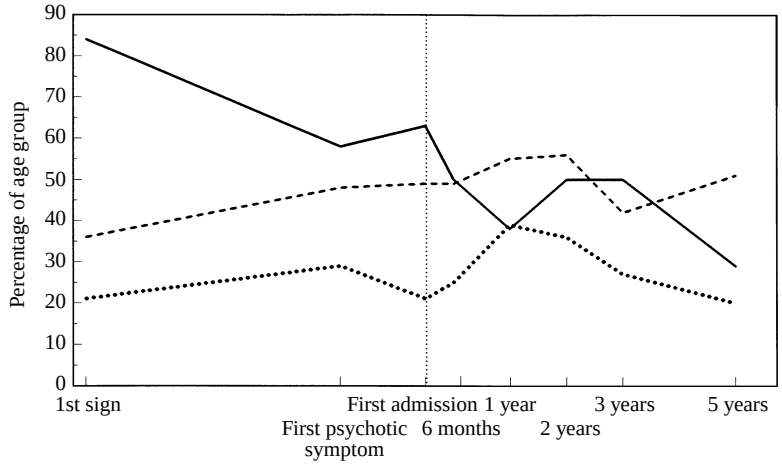

FIG. 5. Social course; financial independence – ABC follow-up sample, $N = 115$ – autonomy: living on own or partner's income. (Age groups: ·····, 12–20 years; – – –, 21–35 years; ——, 36–59 years.)

assessed with the Disability Assessment Schedule, DAS (these findings are not reported here).

As for the social course, Fig. 5 depicts the percentages of financially autonomous patients in the three age groups from the first sign of schizophrenia until the 5-year follow-up. Age had a slightly favourable effect on social outcome, but a strongly unfavourable on the social course: 84% of the late-onset patients, but only 21% of the early-onset patients were earning their living or were housewives when the illness started. About 10 years later (i.e. on average 5 years after first admission) about the same proportion of the early-onset cases as before (20%) were earning their living, but only 29% of the late-onset cases were able to do so, which in this group meant a 55% decrease from the rate of financial autonomy at the onset of schizophrenia.

When long illness courses are studied, the readmission rates are frequently used as indicators of the clinical course, and late-onset patients have usually been found to fare better in this respect. In a proportional hazards model Eaton *et al.* (1992) calculated a significantly reduced relative risk for readmission (0·39) in patients with an onset after the age of 60. Riecher-Rössler *et al.* (1997) corroborated this finding in a study also based on Danish case-register data. The younger the patients at onset, the higher the risk for readmission over a 10-year period. They investigated the hospitalization histories of all the 1160 surviving patients who had been admitted to a psychiatric hospital or day hospital in Denmark in 1976 for the first time with a broad clinical diagnosis of schizophrenia (ICD-9 295, 297, 298.3, 301.83). Over a period of 10 years the oldest group of patients (age > 60) fared best regarding the number of readmissions (on average 2.1 times), time spent in the community until readmission and total time spent in hospital (a mean of 446 in-patient days in 10 years). First admissions under age 40 fared worst in these respects (a mean of 4·3 rehospitalizations and 659 in-patient days).

DISCUSSION

The analyses of the two samples, the population-based ABC first-episode sample under 60 years of age and the clinical CIMH first-admission sample of all ages, coincide in their results on the effects age has on the clinical presentation of broadly defined schizophrenia. No differences between age groups were found for type of onset and early symptom-related course, insidious onsets and negative symptoms prevailing at all ages. Minor age differences emerged for the overall severity of symptomatology, as measured by the PSE-CATEGO scores. These differences were mainly due to a higher rate of non-specific symptoms in the younger patients, particularly in boys. A high score of non-specific syndromes in schizophrenia is probably an indication of the severity of an acute episode, in the same way as fever is in infectious diseases. Hence, as

expected, first episodes seemed to be most severe in early-onset schizophrenia. At later ages of onset they became slightly milder. The different trends of symptom severity in the two sexes (decrease with an age in men, stagnation/partial increase in women) provided additional evidence for the assumed protective effect of oestrogen until pre-menopause.

The psychopathological patterns of the first episodes differed only slightly across the total age range. The slight increase in neurological and psycho-organic symptoms with advanced age is presumably accounted for by co-morbidity with degenerative brain diseases. The results are in concordance with Jeste *et al.*'s (1995) finding that early- and late-onset patients with schizophrenia are similar on most measures of schizophrenic psychopathology and neuropsychology. The core of positive and negative symptoms does not differ significantly between the age groups, except for an interaction with gender (see below). In contrast to Mayer *et al.*'s (1993) and Castle & Murray's (1991) results, affective symptoms, depression in particular, did not differ significantly between early- and late-onset cases.

Considerable age differences emerged regarding the elaboration and systematization of a few positive symptoms, which corroborated earlier studies with smaller samples (e.g. Kay & Roth, 1961; Pearlson *et al.* 1989): a linear increase in elaborated paranoid and systematic delusions with age. This type of delusions contain a cognitive component: with ageing there is a stronger tendency to cope by externalization, that is, to explain failures, mishaps or guilt by external factors. It is well conceivable that developmental changes with increasing age might be responsible for these trends rather than the disease process itself. The role of cognitive maturation in the knowledge of the systems, e.g. electromagnetic rays, included in the delusions as explanatory principles has recently been demonstrated by Galdos & van Os (1995).

The steady decrease over the whole age range in the key symptoms 'incoherence of thought' and 'disordered sense of self', which indicate that disorganizational syndrome dimension and are particularly frequent in early-onset schizophrenia (Remschmidt *et al.* 1994; Häfner & Nowotny, 1995), can also be attributed to developmental factors. Lower stages of cognitive development and a not yet stable personality presumably produce a greater number of cognitively poorly elaborated symptoms and signs of mental disorganization. As indicated by the increase in systematic delusions, the coping abilities at more advanced stages of personality development become more differentiated and increasingly stable, thus, possibly reducing the disorganizing effect of the psychosis.

Some of the age differences, particularly in illness behaviour, can be attributed to gender differences in the development of behaviour. A marked excess of socially negative behaviour (substance abuse, antisocial behaviours, self-neglect) is seen in male adolescents and young male adults compared with women of the same age and older men among both schizophrenics and in population studies (Hambrecht *et al.* 1992; Jablensky *et al.* 1992).

The results presented here shed light on the long-standing discussion about the heterogeneity of delusional/schizophrenic syndromes in old age. In accordance with other papers (e.g. Kay & Roth 1961; Pearlson *et al.* 1989; Howard *et al.* 1993; Almeida *et al.* 1994) the present data convey the impression of qualitative similarities, but quantitative differences between the diagnostic categories of very late-onset schizophrenia and late paraphrenia or non-organic delusional disorder in old age.

As with Fish (1960), Grahame (1984), Howard *et al.* (1993) and others we could not find distinctly discriminating empirical criteria in the spectrum of schizophrenia and paranoid disorders in old age, but instead, clinical syndromes that showed considerable overlap. They do not justify the formation of empirically distinct subtypes or diagnostic categories. The characteristics showing variation between schizophrenia and late paraphrenia or delusional disorders of old age are located on continuous dimensions. The main distinguishing dimension of practical relevance appears to be age itself and, to a far lesser degree, severity of the disorder.

The similarity of the core symptoms of schizophrenia across the age range and between the sexes may have implications for a comprehensive heuristic model. The schizophrenia syndrome, including the genetically related paranoid psychoses might represent one of the few genetically transmitted patterns of response of our brain to various moderately severe dys-

functions. This response pattern, or the underlying dysfunctions, can be triggered by various causes after a certain level of maturity has been reached until very old age and represents, as Jablensky (1988) put it, 'a common final pathway'. Early-onset schizophrenias are frequently associated with preceding pre- and perinatal complications, minor brain anomalies and developmental disorders as risk factors (Castle & Murray, 1991; Done *et al*. 1994; Crow *et al*. 1995; Walker *et al*. 1995; Weinberger & Lipska, 1995). In contrast, many late-onset schizophrenias and paraphrenias might involve relatively mild degenerative brain processes. If both developmental and degenerative processes were capable of triggering schizophrenia or paraphrenia in persons with a genetic liability, early- and late-onset psychosis would be very similar disorders with different underlying causes.

The follow-up data indicate that, despite the great variability of individual courses (an der Heiden *et al*. 1995), age of onset does not have a strong effect on the symptom-related course. Symptom scores in different age groups are fairly similar after the remission of the first psychotic episode. But, because of generally low levels of symptomatology in remitted patients and small sample sizes in some age groups resulting in low statistical power, these results need further validation.

The lower risk for readmission in late-onset cases might reflect a slightly lower severity of the disorder, but very likely also the consolidated social situation and less maladaptive illness behaviour at older age.

At onset the more favourable social status of late-onset schizophrenics is clearly determined by the late intrusion of the disorder into their social biographies, that is, when most patients have completed their social ascent. Due to the better social conditions at onset (also reported by Jeste *et al*. 1995 and others), patients with late onset show slightly better 5-year social outcomes than early-onset cases. But age at onset has a different effect on the social course of the disorder. By the 5-year follow-up after first admission late-onset patients have suffered pronounced social decline from their previous social statuses, whereas early-onset cases on average have mostly retained their (lower) social statuses. Early-onset patients show the highest number of dependent patients from onset until 5 years after first admission, but on average, they suffer stagnation and not social decline. The late-onset group, in contrast, has the lowest number of financially dependent patients when the first sign of the disorder appears. After illness onset, however, and long before first admission, their number increases steadily indicating social decline, also described in case studies (e.g. Harris *et al*. 1988). But this finding does not necessarily apply to old age. After retirement, age of onset is presumably no longer bound to have a comparably strong effect, because income is often guaranteed by inalienable rights and the risk of losing an occupational or social status is clearly reduced in most cases.

The pronounced difference in the social course of early- and late-onset schizophrenia can thus be attributed to three conditions: (1) if onset occurs at early stages of social development, it usually leads to stagnation at the low social level achieved by that time; (2) late-onset patients have accomplished more social roles and hence, on average, have reached higher levels of social development (they have more to lose as a consequence of the disorder than early-onset patients, nevertheless, late-onset patients usually manage to retain some of the acquired social advantages, so that in their case the disorder mostly has a better social outcome than in early-onset cases; and (3) when onset occurs after retirement age, social outcome will presumably be less affected, because the patients have acquired more inalienable rights and in most cases the occupational-status characteristics can no longer be lost.

Conclusions

Our study indicates that the symptomatology and course of non-affective functional psychoses are influenced not only by factors inherent in the disease process, but also by determinants of cognitive, personality and social development. The findings provide strong support for the assumption that age-dependent developmental factors might be responsible for the formation of several mainly delusional symptoms, especially paranoid and systematic delusions in late-onset cases, as well as for the higher frequency of the disorganizational syndrome in early-onset cases. The less mature stages of cognitive and personality development at a young age of onset

seem to be associated with a lower stability of personality and a poorer cognitive ability for well-organized coping with the basic, partly genetically transmitted neuropsychological dysfunctions and impairments. In later life the greater stability of a fully developed personality may offer some defence against mental disorganization, which, together with cognitive maturation, results in the formation of protective delusional systems by way of externalizing the stressing mental experiences (e.g. Galdos & van Os, 1995).

Age-dependent developmental factors are also involved in the production of illness behaviour, which differs markedly between the sexes. Maladaptive illness behaviour, such as substance abuse, dissocial attitudes or self-neglect, reflects patterns of abnormal behaviour typical for young males in general (e.g. Rutter *et al*. 1977) and not specific to schizophrenia.

The disorder itself to some extent seems to account for the association between age of onset and severity of symptoms in the first episode. The neuroendocrine protection provided by oestrogen leads to a higher age of onset and a greater frequency and severity of late-onset schizophrenia in women with decreasing oestrogen secretion (Häfner *et al*. 1991). The strongest age effects after onset are produced by the biological factor age at onset, which interacts with social and psychological developmental factors. Because of the different social conditions at the beginning of the disorder the age differences have a great practical impact, especially in terms of the social consequences of the disorder. Underlying these consequences is the clearly detrimental impact of the disorder on age-dependent processes of social and personality development as well as the fact that illness behaviour, too, depends on developmental factors. After the remission of the first episode indicators closely related to the disorder show stable, parallel courses in both men and women without any observable trend until 5 years after first admission.

Hence, in schizophrenia part of the symptomatology in the first episode, illness behaviour and social course must be understood as a complex process in which disease-inherent factors interact with factors of neurohormonal, psychological and social development, which all relate differently to age. Obviously, age and sex have not only direct but also indirect mediated effects on the clinical picture, social course and outcome of schizophrenia.

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