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EDITORIAL

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Special Issue "Schizophrenia in Childhood and Adolescence"

After decades of stagnation in schizophrenia research, a few steps forward have been made recently and have given rise to new hopes. They are founded above all on new methodological approaches in molecular biology and genetics, in neuroimaging and functional analysis of cerebral blood flow and brain metabolism. Some progress has also been achieved by the revelation of the "hidden" early course and by the systematic epidemiological study of the precursors of this disorder. Together with the concomitant neuropsychological and brain morphological findings in schizophrenia, they have emphasized the topical importance of the neurodevelopmental model of schizophrenia.

Neurodevelopmental model of schizophrenia

The phase of life when possible associations between delayed brain maturation and schizophrenia can best be discovered is childhood and adolescence. Thus the early-onset schizophrenias and their antecedents, which have – similar to late-onset schizophrenias – long been given too little attention, are now coming into the focus of interest. The comparison with the normal development and the transition of preexisting deficits into the manifest disease are essential aspects of the neurodevelopmental model of schizophrenia, although they may not yet be fully understood.

The four contributions of the special issue "Schizophrenia in Childhood and Adolescence" deal with these aspects.[1] They include a controlled epidemiological study of the childhood precursors of schizophrenia, affective psychoses and neuroses (Crow et al.), a multilevel study of early-onset schizophrenia (onset of psychosis by the age of 13 years) and its precursors focusing on neurobehavioural aspects before and after the outbreak of the disease (Asarnow et al.); the third article is dedicated to the epidemiology of early-onset schizophrenia under different definitions of onset and age thresholds (Häfner and Nowotny) with special regard to the prodromal phase and early course. The fourth article comprises a clinical study of the symptomatology and course of early-onset schizophrenia compared with schizophrenia occurring in adulthood (Schmidt et al.).

Schizophrenia: a continuous process?

The results: the great frequency of precursors and the mostly long duration of the prodromal phase prompts the question of whether it is at all possible to delimit the disorder as against its precursors. Could it also be a continuous process such as a state of delayed brain maturation with various functional impairments which, under the influence of stress, leads to decompensation in the form of psychosis? Conventionally defined, however, i.e. according to the criteria sets of ICD-10 or DSM-IV, schizophrenia shows predominantly an episodic course of the psychotic symptomatology and an often progressive course of the negative symptomatology. Its maximum risk of onset is observed during adolescence and early adult age. The psychotic component usually shows a clear first onset with positive symptoms accumulating up to the acute episode. The systematic study of the course prior to the first psychotic episode moreover revealed that approximately 75% of all cases are preceded by a prodromal phase with negative and nonspecific symptoms lasting several years on average (Häfner et al. 1993). Its onset cannot be assessed with the same precision as that of the first psychotic episode; but it can be identified quite dependably as the first sign of the disorder in a time grid. From this moment on schizophrenia develops with increasing accumulation of negative and nonspecific symptoms, and the later-occurring positive symptomatology develops with a steeper increase. There is little doubt that schizophrenia is a disease with an onset and a certain course, not only a state of impairments.

The antecedents of schizophrenia that are associated with a delayed maturation of the brain, be it of genetic or

[1] The Schizophrenia Bulletin issue (Vol. 20, No. 4, 1994) on "Childhood-onset schizophrenia" edited by one of our authors (R.B. Asarnow) was published after the typesetting of this special issue so that its contributions, apart from that of Asarnow, could not be referred to.

exogenous nature, can therefore be timed fairly well in relation to the onset of the disorder. In the later course of the disease, however, they can no longer be distinguished definitely from the disease-dependent impairments. They are significantly more frequent in schizophrenias with onset up to the age of 26 years in comparison with healthy individuals: on the basis of a certain cut-off their frequency is 50% as compared with a base rate of 10% with controls (Crow et al.). These antecedents are a part of schizophrenia theoretically because they are presumably an expression of the same underlying or risk-increasing brain dysfunction, and are a part practically because they can lead to delays or deficits in the cognitive and personality development even before the outbreak of the disease. The possibility that some social consequences of schizophrenia appear early, i.e. prior to the first episode, has some impact on the old controversy between the social causation and the social selection hypothesis. It is of practical relevance also because early-onset schizophrenia is characterized by a more unfavourable social course, at least in its social status components, than medium- or late-onset schizophrenia (Schmidt et al.; Häfner and Nowotny).

Continuity model of functional psychosis?

Crow et al. provide an interpretation of the results of their precursor study on the basis of a comprehensive continuity model covering the total range of all functional psychoses from schizophrenia and schizoaffective disorders through to affective psychoses. The fact that the social outcome as an indicator of the severity of the disorder varies between unfavourable for schizophrenia and fairly good for affective psychoses without any clear cut seems to support this model (Häfner and Maurer 1994). It is further backed by the results of the British Child Development Study (Crow et al.): Deficits in academic performance, social behaviour, emotional reactions and neuromotor development during childhood and adolescence are presented not only by those later developing schizophrenia. The same types of antecedents are found with lower prevalence in children and adolescents later treated for affective psychoses. However, with the group of neuroses a diagnostic category has been included in the continuity model that already goes beyond functional psychoses. The study of this issue on the basis of type and prevalence of the precursors themselves would imply the inclusion of yet further diagnostic categories where such antecedents are found with significant frequency, e.g. mentally retarded or hyperactive children, dissocial personality disorders and other similar disorders.

For the time being, however, presumably because of our limited knowledge of the functional relationship between brain functioning and the psychopathology of functional disorders, we are confronted with two levels of phenomena:

1. Neurobehavioural and neuromotor signs indicative of delayed brain maturation. They occur with low prevalence in normal individuals, somewhat more frequent in minor mental disorders and with high incidence in severe functional mental disorders presenting a continuous pattern of distribution.
2. The second series of phenomena, which seems to be causally related in a still-unknown way with the first, is that of clinically diagnosed diseases or syndromes. Some of these diseases can be clearly distinguished from each other not only on the basis of the conventional diagnostic criteria sets, but also on genetic grounds.

The question of what distinguishes schizophrenia from neighbouring diagnostic groups at both levels is dealt with in this special issue, as well as the more fundamental question of whether the precursors are an expression of the same underlying neurodevelopmental disorder or only unspecific risk factors. They are, however, not yet answered definitely. But the two epidemiological studies on precursors, onset and early course of schizophrenia (Crow et al.; Häfner and Nowotny) and the investigations into the transition from neurobehavioural antecedents to the information-processing deficits of the psychosis (Asarnow et al.), have paved the way towards possible answers.

Precursors as an indication of delayed brain maturation

Deficits in academic performance, social behaviour and emotional reactions in children later developing schizophrenia have been described several times on the basis of school reports, teachers' and parents' judgements and child guidance institutions (Watt 1978; Hartmann et al. 1984; Ambelas 1992). The opportunity to study precursors on a controlled epidemiological basis was provided by the British Child Development Study. The results of the cross sections conducted at the age of 7, 11 and 16 years show for schizophrenics in comparison with normal controls significant differences in neuromotor, cognitive and behavioural functioning, although with a slight tendency to improve for coordination disorders at the age of 16 years. The group of patients admitted for neurosis by the age of 26 years showed slightly fewer impairments and the group of affective psychoses markedly fewer impairments. At the age of 16 years the later affective psychoses have obviously made up for all their development deficits. The findings of Crow et al. are confirmed by the neuropsychological, psychophysiological and neurophysiological studies of Asarnow et al. conducted retrospectively and in cross sections on childhood schizophrenias with onset up to the age of 13 years. They reveal a clearly delayed development in the later schizophrenics starting already during infancy. Particularly at the neuromotor and neuropsychological level they provide clear evidence for the developmental character of the premorbid impairments (Asarnow et al.).

After the outbreak of the first psychotic episode the cognitive deficits occur as demonstrated in numerous studies. They have been assessed by Asarnow et al. at the neu-

ropsychological and EAP levels, and interpreted as the expression of reduced information processing resources because of impaired CNS functioning that is due eventually to the same lesions of the brain as are the signs of neurodevelopmental delay before the outbreak of the psychosis. The childhood psychoses investigated by Asarnow et al. undoubtedly represent "a more homogeneous and severe form of schizophrenia". Of what kind, however, is the presumably underlying lesion of the brain? Asarnow et al. holds that neither its cause nor its localisation are known. Weinberger (1987) suspects it in the limbic system and in the prefrontal cortex. These are the regions indicated by many neuroimaging and EAP findings. Nevertheless, this association has not yet been completely secured, especially concerning the neuroanatomic findings and the scarcely consistent correlations between neuropsychological and brain findings. Crow et al. suspects an interaction between an extrinsic pathogenic and the preexisting brain structure, which together could produce a single developmental process. There is substantial hope that this hypothesis may soon be tested.

Gender differences in precursors, illness behaviour and age at onset

The precursor study by Crow et al. and the epidemiological early onset study by Häfner and Nowotny suggest that even more factors are involved, because precursors as well as beginning schizophrenia both present clear gender differences. At the age of 7 years, although more obvious at 11 years, boys who later develop schizophrenia are characterized by an "overreactive" behaviour pattern with hostility towards adults and towards children, anxiety for acceptance by adults and children, inconsequential behaviour and restlessness. Eleven-year-old girls, on the other hand, differ from normal controls by an "underreactive" pattern with unresponsiveness, social withdrawal and depression, as well as dismissing of adults (Crow et al.).

At the point of the first psychotic episode the early-onset schizophrenics show no significant gender differences in the positive and negative core symptoms of the disorder. Boys, however, exhibit far more often socially negative behaviour compared with the girls who are more socially adapted. Similar gender differences in adolescence are also found in population studies (Esser et al. 1992). Conduct disorders and dissociality are significantly more frequent in boys; emotional disturbances and depressive mood in girls. Obviously, the gender differences in precursors and early symptomatology of schizophrenia are to a great extent due not to the disease or its underlying brain dysfunctions but to gender-specific behavioural patterns in childhood and adolescence. It may be assumed that these gender- and age-dependent patterns of psychopathology have thus far been indiscriminately included in the clinical picture of early-onset schizophrenia.

Childhood psychoses that can later actually be validated as schizophrenias are rare, and even more so the younger the age group (Häfner and Nowotny). Their symptomatology is often less characteristic than that of adult schizophrenia. This finding is confirmed by each of the three contributions dealing with early-onset schizophrenia (Asarnow et al.; Häfner and Nowotny; Schmidt et al.). In these studies also the state of the emotional and cognitive development is presumably reflected in the symptomatology of the psychosis and in the behaviour of the afflicted children and adolescents. It is noticeable that early-onset schizophrenias are nearly always preceded by a lengthy prodromal phase of several years on average. Its symptoms presumably contaminate the precursors assessed during adolescence by the Child Development Study, because this study is based on a sample of patients first admitted for schizophrenia up to the age of 26 years. Were the proportion of already manifest prodromal phases of schizophrenia taken into account, the decrease in developmental deficits on the precursors assessed at the age of 16 years would be even more apparent.

Early disruption of the social biography through the disease

Clinical study of the course of early-onset schizophrenics first admitted to the hospital prior to the age of 18 years (Schmidt et al.) establishes that schizophrenia with early onset takes a less favourable course on average than schizophrenia beginning in adulthood. This repeatedly confirmed finding cannot be questioned at the clinical level. Aspects of cognitive, social and personality development have not yet been investigated extensively in the studies of early-onset schizophrenia. The epidemiological study (Häfner and Nowotny) demonstrates that the disease breaking into the early stages of social development leads to more severe consequences in social status than an outbreak of the disease at a later age when important social roles have already been fulfilled. Except for the higher frequency of unspecific symptoms in early-onset schizophrenia, the core symptoms of the psychosis and the early course seem to present no great differences between the age groups and the genders. It is obviously not the symptomatology and early course that constitutes the most apparent difference between late- or medium- and early-onset schizophrenia, but the early disruption of the social biography and the impaired further social ascent. This means that the less favourable early course of early-onset schizophrenia can hardly be due to age differences in symptomatology and course, but rather to very early disruption of social development. Consequences may be, for instance, an early school leave with impaired cognitive development, insufficient acquisition of secondary social relationships and the inability to qualify for a job and earn a living.

This result coincides with a case register study by Eaton et al. (1992) quoted by Crow et al. that uses the history of inpatient treatment as an indicator of course and outcome: early onset (first admission), male and single status predict readmissions over a period of ten years. But when age at onset is taken into account, neither gender

nor marital status add significantly to this prediction. The impact of the variables male and single status is actually determined by age at onset, because males are first admitted 4–5 years on average earlier than females in the Danish case register, and because the age at onset also has a negative effect on the chances of marriage (Häfner er al. 1994).

The interpretation of Crow et al. is different from ours. They assume that "age at onset is a single variable concerned with timing of a major determinant of the disease", because it is also an important aspect of the development of the CNS and/or of the neurodevelopmental disorder underlying schizophrenia. With increasing age of onset, however, this association disappears. Both hypotheses, the one referring to the disease breaking into an early stage of social development (Häfner and Nowotny) and that of Crow et al., founded on the timing of an underlying retarded neurodevelopmental process, are interesting heuristics that need to be investigated further or replicated. This applies especially to the associations between early-onset schizophrenia and other aspects of individual development: It can be assumed that not only the disruption of the social biography through the disease, which could be rather easily operationalized and studied, but also the time or state of cognitive and personality development at the onset of the illness is essential for its later course. The attainable level of cognitive performance and maturity of the personality could easily be determined, for instance, by the development reached at the outbreak of the disease. In any event, the consideration of developmental processes at neurobiological, social, cognitive and personality levels is likely to provide a more differentiated understanding of early-onset schizophrenia, possibly of schizophrenia in general, and new perspectives for early treatment and rehabilitation.

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