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Long-term outcome of schizophrenia and its neurobiological background

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Similar to other long-term studies, the results of the Munich 15-follow-up study, which compared the outcome of first hospitalised patients with schizophrenic, schizoaffective and affective psychoses, demonstrated that on average the course and outcome of schizophrenia is less favourable than that of affective and schizoaffective disorders. Furthermore, it was shown that at least a subgroup of schizophrenic patients generally have a poor outcome. Negative symptoms occurred in all functional psychoses but were more frequent and prominent in the schizophrenic group than in the two other diagnostic groups at any time of assessment. Narrower concepts of negative symptoms, conceptualised as the deficit syndrome, seem to be specific for schizophrenia and appear quite rarely in patients with affective psychosis. Especially the long-term outcome appears to be predominantly characterised by negative symptoms/the deficit syndrome in the sense that the negative symptoms/deficit syndrome differentiate much better the schizophrenic from the affective/schizoaffective patients than the positive symptoms. While there is such a clear signal that the increase of negative symptoms is the core symptomatology of schizophrenia, the question has not yet been fully answered whether cognitive disturbances, which are generally seen as the most relevant vulnerability indicator of schizophrenia, progressively deteriorate over the long-term course of schizophrenia.

Altogether there is evidence to support Kraepelin's original hypothesis that schizophrenia has a worse outcome than affective psychosis. A subgroup of schizophrenic patients seem to have a more deleterious long-term course and outcome in terms of functional incapacity and psychopathological disturbances. Particularly negative symptoms, and possibly also cognitive disturbances, characterise patients with an unfavourable course.

How does this relate to the current theories and empirical data on the aetiopathogensis of schizophrenia? The neurodevelopmental hypothesis, which is very broadly accepted, can explain the origin of the disease in terms of vulnerability. However, at least in a subgroup of schizophrenic patients with a more chronic deteriorating course, the hypothesis of a progressive neurotoxic/neurodegenerative process has to be taken into consideration. Structural MRI data from several research groups suggest evidence for structural brain changes in the course of the disease. These data are in accordance with our Munich MRI database, which includes altogether data from 400 patients and controls. Additional analyses show that the brain alterations demonstrated by MRI analyses are associated among others with negative symptoms. Of great interest is the link between genetic abnormalities of schizophrenic patients and brain alterations shown by MRI, which will allow a better understanding of the so-called first and second hit. Another view of the possible progressive biological course of schizophrenia is related to the neurotransmitter systems, especially to the glutamate system. The hypothesis of a glutamate "intoxication", which might explain the progressive deterioration, was suggested on the basis of animal research. Last but not least immunological alterations should be investigated much more carefully. Findings from our own group showing the benefits of a comedication of Cox-II-inhibitors and novel neuroleptics are very promising in this respect.