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EDITORIAL

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Schizophrenia and depression

The present Special Issue is dedicated to a systematic analysis of a highly topical issue, the relationship between schizophrenia and depression at the level of 1) similarities and differences in single symptoms, syndromes and illness course (Häfner et al.; an der Heiden et al., this volume), 2) genetic, neurobiological and psychological mechanisms explaining their joint occurrence and course (Maier et al.; Häfner et al.; Birchwood et al.; Krabbendam and van Os, this volume) and 3) mechanisms underlying the antidepressive and antipsychotic properties of 2nd-generation neuroleptics in the treatment of schizophrenia and contributing to our understanding of the functional basis of depressive symptoms in schizophrenia (Möller, this volume).

Behind this issue lies the question whether the traditional Kraepelinian concept of two phenomenologically and nosologically separate disorders or disease entities – affective and non-affective psychoses – is still valid today. It had long been supported by the more or less exclusively antipsychotic and antidepressive effects of the classic neuroleptics and early antidepressants. A thorough analysis of what we today know about the antidepressive properties of 2nd-generation antipsychotics in schizophrenia (Möller, this volume) casts doubt upon this concept.

Factor analyses of the symptom structure of schizophrenic psychosis have shown that depression is a fourth factor besides positive and negative symptoms and disorganisation (Lenzenweger and Dworkin 1996; McGorry et al. 1998; van Os et al. 1999). Epidemiological studies are consistent in showing that depression is one of the most frequent symptom patterns in the general population and in schizophrenia (Wittchen et al. 2000; The WHO World Mental Health Survey Consortium 2004, The ESEMeD/MHEDEA 2000 Investigators 2004). Depression frequently occurs at the onset of the prodromal illness stage and increases in the early course before antipsychotic and antidepressive treatments get underway. It is the disease process itself rather than medications or other external causes that produce depression (Häfner et al.; an der Heiden et al., this volume). Together with negative symptoms and functional impairment, whose onset mostly follows that of depressive symptoms in initial schizophrenia, depression makes up a prodromal core syndrome, which increases in the first psychotic episode and remits simultaneously with psychotic symptoms. Assessed at 12-year follow-up depression is also the most frequent symptom in psychotic relapses. It increases and decreases with psychotic symptoms and predicts more relapses (an der Heiden et al., this volume) and less affective flattening (Häfner et al. 1999). This strong association between depression and psychotic symptoms and indicators of the underlying disease process suggests that depression is an expression of this process.

Attempts to explain the causal association between schizophrenia and depression start with the genetic level (Maier et al., this volume): schizophrenia and depression show cosegregation and cross breeding, though in an asymmetric way as indicated by the weaker risk for schizophrenia in the offspring of persons with unipolar depression. At the molecular level some loci have been confirmed and one susceptibility gene has been identified as common risk factors for schizophrenia, bipolar disorder and presumably also for depression. Birchwood et al. focus on the psychological consequences of the stressful experience of psychosis. Anxiety, in some cases PTSD and in nearly one third of cases postpsychotic depression are seen by the authors as consequences of inadequate appraisal of and dysfunctional coping with the stress caused by psychosis. The cognitive paradigm proposed by Krabbendam & van Os goes one step further. It proceeds from an at-risk stage for

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psychosis. In their population-based sample of "vulnerable" individuals who reported single hallucinatory symptoms without suffering from psychotic illness depression was associated with a significantly higher frequency of BPRS-defined psychosis at three-year follow-up compared with non-depressed controls. The authors explain the increased risk for psychosis as caused by depression-related inadequate appraisal of or deficient coping with hallucinatory symptoms.

These sources provide three probably related explanatory models of depression in schizophrenia: a genetic, a cognitive, which follows the Vulnerability Stress Coping Model (Birchwood et al.; Krabbendam and van Os, this volume), and a neo-Jacksonian, which explains depression as a preformed psychopathological and/or neurobiological reaction pattern of the human brain or mind. This reaction pattern is characterised by a lower threshold of precipitation and can be triggered by various kinds of factors, such as psychological stress, mild dysfunctioning or early stages of dysfunctional or degenerative processes of the human brain – including schizophrenia – (Häfner et al., this volume). Hence, depression is interpreted as a prodromal stage of a great number of different types of dysfunctional or neurodegenerative processes which are frequently followed by more severe patterns such as psychosis, confusional states and dementia. But we cannot yet tell which of these three models has the greatest explanatory power and to what extent they contribute to explaining the association between depression and schizophrenia.

Focusing on the therapy of depressive symptoms in schizophrenia Möller in his contribution provides an exhaustive overview of the agonistic and antagonistic receptor affinities and diagnosis-independent antidepressive effects of 2nd-generation antipsychotics in the therapy of schizophrenia. These issues, too, are not yet fully resolved. But we already know that the antidepressive potential of the 2nd-generation antipsychotics seems to be related to different pharmacological mechanisms and to differ from the way their antipsychotic effects are brought about. These same mechanisms might also be responsible for the reduction of cognitive impairment.

This, again, brings to mind the prodromal core syndrome consisting of depression, negative symptoms and cognitive impairment, recurring and remitting with psychotic relapses. Several of the 2nd-generation antipsychotics offer opportunities of successfully treating the full spectrum of schizophrenia symptoms, though with very different effects: psychosis, depression, negative symptoms and cognitive impairment (Möller, this volume). Hence, several bridges seem to exist between the two symptom patterns, psychosis and depression. They co-occur, often successively, in progressing brain dysfunction and are frequently caused by the same underlying process.

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