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Schizophrenia and depression: Challenging the paradigm of two separate diseases—A controlled study of schizophrenia, depression and healthy controls☆

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Abstract

Background: We studied descriptive and causal associations between schizophrenia, depressive symptoms and episodes of depression.

Methods: Untreated psychotic, depressive and negative symptoms were assessed retrospectively from onset until first admission using the IRAOS in a population-based sample of 232 first episodes of schizophrenia. A representative subsample of 130 patients, studied retrospectively until onset and followed up prospectively over 6 months after first admission, were compared with 130 age- and sex-matched healthy population controls and with 130 equally matched first admissions for unipolar depressive episodes.

Results: The lifetime prevalence of depressive mood (≥2 weeks) at first admission for schizophrenia was 83%. The most frequent initial symptom of schizophrenia was depressive mood, appearing more than 4 years before first admission and followed by negative symptoms and functional impairment. Showing considerable overlap in symptoms and functional impairment at their initial stages, schizophrenia and unipolar depression became clearly distinguishable with the emergence of psychotic symptoms. In the first psychotic episode 71% presented clinically relevant depressive symptoms, 23% fulfilled the ICD-10 criteria for a depressive episode. With remitting psychosis the prevalence of depression, too, decreased. The high

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frequency of depressive symptoms at the prepsychotic prodromal stage and their increase and decrease with the psychotic episode suggests that depression in schizophrenia might be expression of an early, mild stage of the same neurobiological process that causes psychosis.
Conclusions: The high prevalence of depression in the population and the diversity of its causes prompted us to speculate about a hierarchical model of preformed dimensional patterns of psychopathology.

Keywords: Depression; Prodrome; Schizophrenia; Early course; Sequence of stages; Paradigm of hierarchical symptom patterns

1. Introduction

Unipolar depression is a frequent comorbidity disorder of schizophrenia. The prevalence figures reported from numerous studies vary a great deal: According to a review by Siris and Bench (2003) prevalence rates range from 6% to 75% with a modal value of 25%. Reasons for this pronounced variance are: 1) whether diagnoses, syndromes or single depressive symptoms are being looked at, 2) whether point or lifetime prevalence rates are used and 3) the illness stage of schizophrenia studied.

Schizophrenia and unipolar depression share some of their risk factors and precursors.

1) Unipolar depression shows genetic overlap in the offspring of parents suffering from schizophrenia (Kendler et al., 1993, 1996; Maier et al., 1993, 2002). In the New York High-Risk Study Erlenmeyer-Kimling et al. (1991) found that 18% of the offspring (N=73) of mothers with schizophrenia developed schizophrenia and 7% affective psychosis by age 26 years. Molecular-genetic research has identified one gene (G30/G72 in 13q candidate region) which seems to be involved in both schizophrenia and bipolar disorder (Maier et al., 2005).
2) Pre-, peri- and postnatal complications of brain development are risk factors for both disorders, but more prevalent and more severe in schizophrenia than depression (Jones et al., 1994, 1998; Elkis et al., 1995; Marcelis et al., 1998; Van Os et al., 1999c).
3) Structural brain abnormalities constitute risk factors for both schizophrenia and depression: mild loss of brain volume mainly in the prefrontal and temporal cortex and the hippocampus area (Jones et al., 1994; Elkis et al., 1995; Hirayasu et al., 1998; Weinberger, 1999; Heckers et al., 2002).
4) Psychosocial stress is a well-established precipitant of depressive illness and of psychotic relapses in schizophrenia, but not sufficiently replicated as a precipitant of first-episode schizophrenia (Dohrenwend et al., 1995; Bebbington et al., 1993).
5) Certain personality traits, such as neuroticism (Maier et al., 1994; Van Os et al., 2002), and subtle impairment in social, interpersonal and cognitive abilities in childhood and adolescence are precursors of both schizophrenia and depression (Done et al., 1994a,b; Van Os et al., 1999c; Jones and Done, 1997).

The effect sizes of all these risk factors, except psychosocial stress, in persons with depression occupy an intermediate position between those in probands with schizophrenia and healthy subjects.

The dimensional structure of the full symptoms of schizophrenia comprises besides Liddle's (1987a,b; Liddle and Barnes, 1990) three factors–positive (reality distortion), negative (psychomotor poverty) and disorganisation–depression as a fourth factor (Kitamura et al., 1995; McGorry et al., 1998; Van Os et al., 1999a,b; Löffler and Häfner, 1999).

Verdoux et al. (1998) and Van Os et al. (1999c) have shown that psychosis is a dimension continuously distributed in the general population, ranging from one single psychotic symptom in healthy individuals to full-blown psychosis in need of treatment.

The dimension "depressed mood", also continuously distributed in the general population, is highly significantly associated with the psychosis dimension only in schizophrenic psychosis. Less severe psychopathology on the depression dimension–subthreshold depressed mood and single depressive symptoms in mentally healthy individuals–seem to be widespread in the population and independent of the psychosis dimension.