Discrete and continuous approach in the conceptualization of bipolar disorder and schizophrenia

*Cyril Höschl and Pavla Stopková*

**Summary**

Validity of the current diagnostic distinction of bipolar affective disorder and schizophrenia in classification systems ICD-10 and DSM IV is challenged by an accumulating amount of various independent findings. The authors review the similarities and distinctions between both disorders in a range from psychopathology to neuroimaging methods. An emphasis is given on genetic findings as a major source of evidence of an overlap between bipolar disorder and schizophrenia. Presumably, a combination of common genetic factors with additional genetic and other illness-unique factors is necessary for development of either disorder.

**Introduction**

In current classification systems ICD-10 and DSM IV, bipolar disorder and schizophrenia are recognized as two separate disorders with distinct presentation, etiology and treatment. This distinction stems in Kraepelin's definition of „dementia praecox“ and „mania depressive psychosis“ and in psychiatric diagnostics appears more than 100 years. Lately, accumulating evidence for shared genetic risk for both disorders suggests a certain degree of causal continuity of bipolar disorder and schizophrenia. This report offers an overview of current genetic findings in bipolar disorders and schizophrenia and summarizes corresponding and distinct results from psychopathology to neuroimaging studies (*Stopková and Höschl*, 2007).

**Psychopathology**

Schizophrenia is a psychotic disorder while bipolar disorder is classified as an affective disorder. However, both mania and depression may be accompanied by psychotic symptoms and vice versa, depression is present in first episode of schizophrenia in 75% of patients. Overall, both disorders may manifest with psychotic symptoms including mood-incongruent symptoms, with disturbed mood, and with catatonia. Furthermore, positive symptoms of schizophrenia are analogous to manic symptoms of bipolar disorders and negative symptoms may correspond to depressive symptoms. Possible relationship between positive and manic and between negative and depressive symptoms is supported by a study of *Kravariti et al.* (2005), which found evidence that executive dysfunction in patients with psychotic disorders may be more related to their symptom profile than their diagnosis.

**Comorbidity**

In studies of mortality and morbidity, bipolar disorder and schizophrenia share high suicidality, cardiovascular diseases, obesity, diabetes and drug abuse.

**Epidemiology**

Both disorders are worldwide, lifelong, and recurrent illnesses with periods of exacerbation and partial or full remissions. Lifetime prevalence of schizophrenia and
bipolar disorder type I is around 1%. Women and men are affected at approximately equal rates and the typical age of onset is similar. Both disorders also share risk factors showing evidence for impaired prenatal development, such as birth seasonality, abnormal dermatoglyphs and higher incidence of perinatal complications. However, there is evidence for differences in prevalence in geographical isolates, in presence of minor physical abnormalities and possibly also in influence of psychosocial factors, urbanicity and use of cannabis.

However, based only on similar epidemiological parameters, it is not possible to assume any degree of continuity between bipolar disorder and schizophrenia. The main evidence for partially shared pathophysiology is given by genetic studies.

**Genetics**

Bipolar disorder and schizophrenia are complex disorders, with multiple genes interacting with environmental factors. Twin, adoption, and family studies suggest high heritability around 80% for both disorders.

Family studies show that both disorders are transmitted in families, moreover, relatives of patients with bipolar disorder have an increased risk for developing schizophrenia and relatives of patients with schizophrenia are also more likely to develop bipolar disorder. Schizoaffective disorder is more common in families of bipolar and schizophrenia patients and both disorders are found more often in families of schizoaffective probands (Craddock et al., 2006).

Both chromosomal aberrations identified in a larger number of psychiatric patients are associated with development of bipolar disorder as well as schizophrenia. One of them is a balanced reciprocal translocation between chromosomes 1 and 11 identified in a Scottish family and the other is an interstitial deletion of 3 million base pairs on chromosome 22q11 manifesting as the velocardiofacial syndrome.

Linkage studies of bipolar disorder and schizophrenia give strong evidence for a partial overlap between predisposing chromosomal regions (Owen et al. 2004, Baron 2002). Recently, several candidate genes emerged from systematic molecular genetic search for specific genes in loci with positive linkage results for schizophrenia. Subsequently, some of these genes were also confirmed in association studies of bipolar disorder. Genes with strongest evidence of involvement in both bipolar disorder and schizophrenia include *dysbindin*, *neuregulin 1 (NRG1)*, *Disrupted in Schizophrenia 1 (DISC1)*, and *G72/G30* (Craddock et al., 2006). Findings available for these candidate genes offer another strong evidence for a common genetic susceptibility across the bipolar and schizophrenia border.

Results of gene expression studies suggest possible mechanisms in pathogenesis of bipolar disorder and schizophrenia. Abnormalities of myelin and oligodendrocyte-related gene expression seem to be a common finding for both disorders.

**Neuropsychological findings**

Patients with schizophrenia have widespread cognitive abnormalities (*Heinrichs and Zakzanis, 1998*). More specific deficits described in schizophrenia include impairment of executive functions and both long-term and working memory. Cognitive deficit in schizophrenia is present during acute episodes as well as during remissions. Patients with bipolar disorder demonstrate impairment of cognitive functions during an affective episode with psychotic symptoms. However, during periods of remission, bipolar patients tend to have better results in majority of cognitive tests than patients...
with schizophrenia and their cognitive functions are preserved with some possible exceptions, e.g., verbal memory (Quraishi and Frangou, 2002).

**Childhood development**
The development of schizophrenia is preceded by childhood developmental impairments in the areas of cognition, language, motor performance, social, emotional and behavioral development (Cannon et al., 2002). In affective psychosis, developmental impairment does not have such a strong effect and is likely confined to early-onset cases (van Os et al., 1997). Few studies aimed at children who were later diagnosed with bipolar disorder or mania show that there is no preceding developmental impairment. Greater cognitive impairment in schizophrenia compared with bipolar disorder is also evidenced by the Dunedin birth cohort study.

**Neuroimaging studies**
Imaging studies of schizophrenia show an overall decrease in brain volume and enlargement of lateral and third ventricles. In bipolar disorder are no changes in brain volume and larger ventricles were found only in bipolar patients with more severe illness or multiple episodes. In affective psychosis, enlargement of ventricles is described, but of a lesser degree than in schizophrenia. The most interesting differences concern the temporal lobe. Schizophrenia is characterized by reductions in the volume of the temporal lobe, hippocampus and amygdala. In bipolar disorder, the results are inconsistent and include enlargement of temporal lobe, no changes in hippocampus, and both enlargement and reduction of amygdala.

**Pharmacotherapy**
Both common and distinct features can be found in acute as well as long term pharmacotherapy of both disorders. For example, there are differences in acute treatment of both disorders – neuroleptics are not effective in the treatment of depression and monotherapy with lithium and antiepileptics is ineffective in the treatment of schizophrenia. The main overlap concerns some atypical antipsychotics with their antimanic, antidepressive and mood stabilizing effects. There are also considerable similarities between both disorders in non-pharmacological procedures, such as electroconvulsive therapy and transcranial magnetic stimulation.

**Conclusion**
Partially shared predisposition for bipolar disorder and schizophrenia is consistently supported by family, linkage, and molecular genetic studies. A shared predisposition is presumably underlying common pathophysiological mechanisms, which are reflected e.g. in analogous symptomatology and treatments effective for both disorders. For development of fully expressed disorder, a combination of common and specific illness-unique factors may be necessary. These distinctive factors lead not only to differences in clinical presentation and treatment of both disorders, but in patients with schizophrenia result in higher impairment in development and in cognitive functions and in more obvious brain structural abnormalities.

Supported by grant IGA MZ ČR NR8564.
Prof. MUDr. Cyril Höschl, DrSc., FRCPsych.
MUDr. Pavla Stopková, PhD

Affiliation: Prague Psychiatric Center and 3rd Medical Faculty, Charles University, Prague, Czech Republic
Address: Prague Psychiatric Center, Ustavni 91, Prague 8 – Bohnice, 181 03, Czech Republic

References: