Introduction to the Special Section

New advances in the understanding and treatment of bipolar disorder

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Abstract
The current renewed interest in the field of bipolar disorders can be attributed to various factors which are reviewed in this Special Section of the International Journal of Neuropsychopharmacology. Bipolar disorders are one of the most frequent disorders in psychiatry and this Special Section presents papers on recent advances in the clinical course, epidemiology, biological models and neurobiology of bipolar disorders. Novel therapeutic approaches will be covered in a second part in Volume 6, Number 3 (September 2003).

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This Special Section of the International Journal of Neuropsychopharmacology reviews the factors behind the current renewed interest in bipolar disorders. Although the incidence of bipolar disorder in the general population was previously estimated at 1–2%, epidemiological data from recent studies which take into account all the entities of the bipolar disorder spectrum, reveal a lifetime prevalence of approx. 5–6% (Angst and Gamma, 2002; Hirschfeld et al., 2003). These figures make bipolar disorders one of the most frequent disorders in psychiatry. According to these studies, hypomania remains a poorly recognized phenomenon, particularly in teenagers and young adults (Angst and Gamma, 2002). Recognition of the enormous burden of depressive states among bipolar patients also represents a significant move forward and challenges future therapeutic approaches. This is part 1 of a Special Section which presents review papers on recent advances in the clinical course, epidemiology, biological models and neurobiology of bipolar disorders. It will be followed in Volume 6, Number 3 (September 2003), by a second part on novel therapeutic approaches.

(1) Recent findings on the clinical subtypes of bipolar disorders are reviewed by Judd et al. (2003), focusing on long-term course and outcome of bipolar I vs. bipolar II disorders. This is the first detailed comparison of the weekly symptomatic status of BP I and BP II patients during a mean of approx. 13 yr of follow-up. The study confirmed that although BP I is more severe, BP II with its intensely chronic depressive features is not simply the ‘lesser’ of the bipolar disorders, but is a more serious illness than previously thought (for instance, as described in DSM-IV and ICD-10).

(2) The complex concept of comorbidity is revisited by Sasson et al. (2003). This paper addresses several relevant questions in bipolar disorder. The first relates to the rate of comorbid Axis I disorders across diagnostic subtypes (e.g. BP I vs. BP II). The second is the effect of Axis I psychiatric comorbidity on phenomenology, course, outcome and treatment response. This paper also reviews the relevant literature on comorbidity in bipolar disorder. It is striking to learn that 65% of bipolar patients have a comorbid diagnosis. The high comorbidity of anxiety and bipolar disorders is discussed in term of therapeutic dilemma.

(3) The natural course and burden of bipolar disorders is reviewed by Wittchen et al. (2003). The paper summarizes our knowledge about the natural course of bipolar disorder, highlighting the gaps in certain fields, such as the age of onset of the disease, the evolution of chronicity and spontaneous remissions, the role of comorbidity and specific functional impairment. The authors
emphasize the need for conducting epidemiological studies in the community that are of key importance for resolving the critical issues of threshold definitions in the context of the bipolar spectrum concept. There is a clear need for identifying the most relevant risk factors for the first onset and illness progression in the early stages, before they come to clinical attention.

(4) The chromosomal regions and genes of interest already investigated for bipolar and unipolar affective disorders are summarized by Oswald et al. (2003), emphasizing the complexity of the genetics of these disorders. The paper also provides a review on the genetics of one of the most important phenotypes in affective disorders, suicidal behaviour. In light of the available data, the authors discuss the reasons for the lack of unambiguously detected locus of interest and put forward some suggestions for future research.

(5) Over the past two decades, brain-imaging studies in bipolar and unipolar mood-disorder patients have examined the pathophysiological mechanisms possibly involved in these disorders. The paper by Soares (2003) provides a comprehensive review on in-vivo brain-imaging studies that examined bipolar disorder patients. The available literature suggest that there are subtle anatomical changes in sub-regions of the prefrontal cortex, medial temporal lobe, and cerebellum, and functional abnormalities in brain circuits interconnecting these same brain regions and the striatum in patients suffering from bipolar disorder.

(6) Understanding the molecular and cellular mechanisms by which mood stabilizers achieve their therapeutic action, especially their shared effects, represent a valuable step in clarifying the pathophysiology and possibly the pathogenic processes that lead to mania and bipolar depression. It is becoming more and more evident that rather than looking for a single mode of action, many different sites of actions should be integrated to obtain a cohesive picture of how neuronal function is modulated by long-term exposure to mood stabilizers (Brunello and Tascedda, 2003).

(7) The study of neuroendocrine abnormalities in unipolar and bipolar affective disorders has been a focus of interest in the past few years (Linkowski, 2003). The modern approach to hormonal dynamics focuses on the circadian and pulsatile profiles that truly represent physiological modulation. Such studies aim to clarify the control and significance of the temporal sleep and wake fluctuations of neuroendocrine system activities. Twenty-four-hour hypersecretion of cortisol, diurnal hypersecretion of growth hormone, and normal 24-h levels of prolactin have been reported in careful chronobiological studies of depressed patients, along with sleep recordings. A disorder of circadian time-keeping seems to characterize acute episodes of major endogenous depression in some patients. This abnormality as well as the associated increases in adrenocorticotrophic and somatotropic activities seem to be a state-dependent rather than trait-dependent phenomenon.

(8) As reviewed by Bowden (In Press), treatment of bipolar disorder is complicated by the multiple phases of the illness, dimensional symptomatology that varies considerably across individuals, and a limited spectrum of activity for all mood stabilizers. Clear guidelines are available for the treatment of acute mania. However, for issues, such as which treatment to use when lithium or valproate are inadequate as monotherapy, evidence is incomplete, and usually derived from both smaller and less well-designed studies. From the data reviewed (Bowden, In Press), for mania, the spectrum of efficacy of valproate is broader than for other mood stabilizers. Maintenance treatment studies support the efficacy of lithium, valproate and lamotrigine, although with different spectra of benefits and limitations for each. These and other promising areas for research-based advances are summarized in the paper.

(9) As reviewed by Ertugrul and Meltzer (In Press), antipsychotic drugs are effective in the treatment of acute mania and as maintenance treatment for bipolar disorder. While both typical and atypical antipsychotic drugs are able to diminish manic symptoms, agitation, and aggression in acute mania, the atypical antipsychotic drugs enjoy a number of advantages, including significantly less extrapyramidal symptoms, diminished risk of tardive dyskinesia, lack of increase in serum prolactin levels (with the exception of risperidone), improvement in cognition, and possible decrease in suicidality. The authors provide evidence that atypical antipsychotic drugs are recommended for use in bipolar disorder as acute treatment, maintenance treatment, and in treatment-resistant patients.

(10) There is an emerging consensus that the greatest unmet need in bipolar disorder is the management of depressive symptoms and the major depressive episodes associated with the disorder.
(Muzina and Calabrese, In Press). The completion of three recent large-scale, double-blind controlled acute trials in BP I depression, summarized in the paper by Muzina and Calabrese (In Press), has improved our understanding of the management of major depressive episodes associated with bipolar disorder. Lamotrigine has been shown to be superior to placebo, paroxetine augmentation has been shown to be better than placebo but only in patients with lower levels of lithium, and moclobemide was similar in efficacy to imipramine (Muzina and Calabrese, In Press).

An emerging literature indicates that mania can be identified in a substantial number of referred children using systematic assessment methodology. Children with mania frequently demonstrate an atypical picture by adult standards with a chronic course, severely irritable mood, and a mixed picture with depressive and manic symptoms co-occurring (Biederman et al., In Press). Most children with childhood-onset mania also have ADHD, which requires additional treatment. Initial clinical evidence suggests that atypical neuroleptics may play a unique therapeutic role in the management of such youth. High levels of comorbidity with other disorders is common, further requiring the cautious use of a combined pharmacotherapy approach. As suggested by Biederman et al. (In Press), more research is needed to build a scientific foundation for the notion that paediatric mania is a unique developmental subtype of bipolar disorder.

References


