New Drug Developments for Bipolar Mania

December 12, 2012  |  Bipolar Disorder
By Daniel C. Mathews, MD, Ioline D. Henter, MA, and Carlos A. Zarate Jr, MD

Bipolar disorder (BP) is a chronic, debilitating illness that affects 0.4% to 4% of the US population. The first nosological efforts describing BP appeared in the early 2nd century and culminated in Kraepelin’s eloquent description of its phenomenology in his 1921 textbook on manic-depressive insanity. Nevertheless, the course and underlying pathophysiology of BP remain elusive.

The disorder is frequently unrecognized, misdiagnosed, and not optimally managed. Moreover, no agent has been specifically developed on the basis of an understanding of the pathophysiology of the illness or mechanism of action of effective treatments.

The current gold standard treatment for BP is lithium, whose mood-stabilizing effects are believed to occur via distinct cellular signaling pathways/targets, such as glycogen synthase kinase 3 inhibition (considered to regulate cellular apoptosis), and other potential downstream cellular mechanisms. In addition to lithium, valproate, and carbamazepine, several atypical antipsychotics (including aripiprazole, asenapine, and cariprazine) are FDA-approved for the treatment of acute bipolar mania (Table).

While these drugs have certainly provided relief for many individuals with BP, significant issues with tolerability and efficacy remain. For instance, clinicians may find themselves in situations in which better-tolerated agents are less effective, and vice versa. In addition, balancing efficacy with adverse effects that affect adherence, such as sedation and weight gain, underscores the urgent need to develop novel and more effective treatments.

Recent clinical findings

Findings from a meta-analysis indicate that the following agents were more effective than placebo for mania: aripiprazole, asenapine, carbamazepine, cariprazine, haloperidol, lithium, olanzapine, paliperidone, quetiapine, risperidone, tamoxifen, valproate, and ziprasidone. Limited data suggest large effect sizes for carbamazepine, cariprazine, haloperidol, risperidone, and tamoxifen.

Another large meta-analysis evaluated the comparative efficacy of aripiprazole, asenapine, carbamazepine, valproate, gabapentin, haloperidol, lamotrigine, lithium, olanzapine, quetiapine, risperidone, topiramate, and ziprasidone at therapeutic doses for treatment of acute mania. The study concluded that antipsychotic drugs were significantly more effective than mood stabilizers; olanzapine, risperidone, and quetiapine were better tolerated than haloperidol. Risperidone, olanzapine, and haloperidol were particularly efficacious. Most of the trials were short (typically 3 weeks), and therefore caution is needed when extrapolating the results to clinical practice. It is also important to note that because of informed consent and general enrollment issues with manic patients, more severe cases were invariably excluded.

Because strong evidence exists for the use of lithium—and to a somewhat lesser extent, lamotrigine and valproate—...
as a maintenance treatment for BP, antipsychotics may be increasingly used to treat the acute manic phase of the disorder and mood stabilizers (particularly lithium) may be used for long-term treatment. Nivoli and colleagues reviewed the major guidelines for the treatment of manic/hypomanic and mixed episodes and found that all guidelines agreed that concurrent antidepressants should be stopped during a manic/mixed episode.

This is a very good article, but every time I read 'BP' I automatically think 'blood pressure'. It's very distracting. The most standardized abbreviation for bipolar affective disorder is BPAD. BP could be a number of things - most would think blood pressure, but also borderline personality. Speaking a common language is subtle but crucial in scientific communication as evidenced famously in psychiatry by the trans-atlantic study years ago. This misuse of an abbreviation detracts from an otherwise good article and degrades good communication.

I agree--thanks for making that observation.

Colin McIver (not verified) @ Sat, 2013-01-12 02:00

I agree--thanks for making that observation.

Cynthia (not verified) @ Wed, 2013-05-29 14:46

I disagree. As somebody who has done a tremendous amount of research on neuropsychology primarily related to bipolar disorder, in my experience, I've found it to be a very commonly used abbreviation. Although it can sometimes get confusing with borderline personality disorder (which is more often abbreviated "BPD"), BP is likely to be referring to bipolar disorder in mental health related articles. For me, personally, that's the first thing I think when I see BP.

Jessica (not verified) @ Fri, 2013-05-31 23:10

The problem is that not everyone has that same instantaneous association. One of the goals of effective communication is to help the reader parse a sentence fluently. It's not worth the 16 characters you save by abbreviating.

*communication

Geoffrey (not verified) @ Tue, 2013-06-04 12:16

This was a very informative article. However, I can not find the list of references.

Per Bergsholm
Dpt of Mental Health Services
Oslo University Hospital at Ullevål
Where can I find the references for this article?

Per (not verified) @ Sat, 2013-06-01 06:38

Kelly (not verified) @ Mon, 2013-06-03 08:38

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