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Learning Objectives

After reading these articles, you should be able to:

1. Discuss the benefits and risks of medications currently used to treat patients with bipolar disorder.
2. Describe the challenges in assessing, diagnosing, and treating bipolar disorder.
3. Summarize some of the current findings in the literature regarding psychiatric treatment.

The Bipolar Spectrum: Practical Tips for Diagnosis and Treatment

Chris Aiken, MD. Director of the Mood Treatment Center and instructor at the Wake Forest University School of Medicine. Co-author, with Jim Phelps, of Bipolar, Not So Much (W. W. Norton & Company).

Dr. Aiken has disclosed that he has no relevant financial or other interests in any commercial companies pertaining to this educational activity.

In this article, Dr. Aiken draws on his vast clinical experience to help us recognize the different types of patients who might present some degree of bipolarity, then provides tips on evidence-based treatments.

Bipolar disorder has long been controversial in the field. Is it overdiagnosed or

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In Summary

- Estimates of the number of patients on the bipolar spectrum have increased dramatically with inclusion of antidepressant-induced mania/hypomania and depression with mixed features in DSM-5.
- Patients with a history of unipolar depression that present with depressive mixed states should be treated as if on the bipolar spectrum.
- For bipolar and unipolar patients, the risk of worsening on antidepressants increases with the severity, duration, and recency of manic or mixed symptoms.

Q&A
With
the Expert

Understanding the Bipolar Spectrum: Tips on Diagnosis

Chris Aiken, MD

Dr. Aiken has disclosed that he has no relevant financial or other interests in any commercial companies pertaining to this educational activity.

TCPR: Dr. Aiken, before we get into some of the controversies about the bipolar spectrum, can you give us a brief history of bipolar disorder?

Dr. Aiken: Certainly. The modern conception of bipolar disorder dates to the early 20th century, mainly to German psychiatrist Emil Kraepelin, who was a very astute observer. Kraepelin noticed that some patients in his psychiatric hospital had a chronic psychosis, which he labeled “dementia precox” (we now call it schizophrenia), whereas others had episodic psychosis, usually with some mood disorder, and these he labeled “manic-depressive psychosis.” This large category included some patients that we would now recognize as having “pure” unipolar depression, some with bipolar disorder, and many who were somewhere in between these extremes.

TCPR: So, it sounds like Kraepelin was the original proponent of the bipolar spectrum idea!

Dr. Aiken: In a sense he was. He believed that depression and mania were part of a “single morbid process,” and interestingly, this was the mainstream conception of manic depression until 1980 and DSM-III. If you look at



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underdiagnosed? Does a “bipolar spectrum” truly exist, or is it a marketing tool for pharmaceutical companies that want you to prescribe more atypical antipsychotics?

At a minimum, the bipolar spectrum includes those patients who meet criteria for both bipolar I and II disorder, which accounts for roughly 16% of depressed patients. But DSM-5 changed that percentage drastically to include two new conditions on the spectrum: antidepressant-induced mania/hypomania and depression with mixed features.

Adding in these patients, the prevalence of bipolar spectrum among depressed patients skyrockets to 41%. Moreover, it rises to 47% when we include depressed patients with short-duration hypomania (a condition in the appendix of DSM-5). Those figures are estimates derived from two international studies with a total N of over 8,000 patients, and they are consistent with other estimates that place

Depression With Mixed Features: Diagnostic Tips	
Manic Symptom	Common Mixed Presentation
Elevated mood or energy	Mood is labile but rarely euphoric. The elevated energy feels uncomfortable—“wired, restless, crawling out of my skin”—and can resemble akathisia.
Impulsivity	It often has a reckless or depressive tone (eg, quitting relationships or jobs, breaking things, aggressive driving, self-harm, and—in the worst case—suicide). When pleasurable in nature, patients may explain away the impulsivity as an attempt to relieve depression (eg, hyperspending through “retail therapy,” binge eating, addictions, or pornography).
Decreased need for sleep	When sleep is decreased in quantity, patients usually still feel they need it, either because of depressive fatigue or because they dread consciousness.
Increased confidence	Patients are demanding or intimidating, or demonstrate undue certainty in their beliefs.
Racing thoughts	Patients’ minds are “crowded” with depressive or anxious thoughts.
Rapid or pressured speech	This is similar to classic mania, but often has a desperate, urgent tone and is associated with dramatic expressions of suffering.
Irritability, distractibility, and motor agitation	Although common in mixed states, these symptoms do not count toward the diagnosis in DSM-5 because they are common in many other disorders as well.

the bipolar spectrum at 40%–50% of depressed patients (Nusslock R and Frank E, *Bipolar Disord* 2011;13(7–8):587–603).

These figures may sound preposterously high to some clinicians, but to be clear, being on the bipolar spectrum is not the same as having “bipolar disorder.” Instead, it reflects the growing realization that mood disorders should not be split into arbitrary categories. Indeed, David Kupfer, the DSM-5 chair, wrote that depression and bipolar are part of “a continuum, with variable expressions of vulnerability to hypomania or mania” (Phillips ML and Kupfer DJ, *Lancet* 2013;11(381):1663–1671).

Clinically, what does all this mean? As a specialist in bipolar disorder, I am convinced that many more patients fit on the bipolar spectrum than we realize. In this article, I will describe five common types of patients who may not appear “bipolar” at first glance but who likely fall somewhere on the spectrum. If you can learn to recognize these patients, you will likely be able to fine-tune your treatment approach and have more therapeutic success.

Depressive mixed states

Typical patient statement

“It’s the worst depression I’ve ever had. I can’t shut my mind off—it races from one dreadful thought to another. The anxiety is unbearable. Everything gets on my nerves. I’m tired and depressed in the day, then

wired at night—driven to do something, but I don’t know what to do.”

Diagnostic tips

The “mixed features specifier” in DSM-5 applies to unipolar and bipolar patients who have 3 or more manic symptoms during their depression. What does this mean? Patients with a history of unipolar depression and without a history of manic or hypomanic episodes do not qualify as bipolar disorder. However, many of these people will present with depressive episodes that include some manic symptoms. These are called “depressive mixed states.” Does this mean such patients are on the bipolar spectrum? In my view, it does, because you will treat them differently from patients who present with a standard depressive episode.

According to a meta-analysis involving 20,000 patients (Vázquez GH et al, *J Affect Disord* 2018;225:756–760), a significant minority of unipolar patients (25%) have depression with mixed features. Because they don’t look like the manic symptoms that we are used to seeing, these mixed-manic symptoms can easily be missed.

For example, when we think of elevated energy in bipolar disorder, we often think of increased productivity. But when mixed with depression, this energy leads to directionless, disorganized

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The Bipolar Spectrum: Practical Tips for Diagnosis and Treatment

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activity. Similarly, rather than experiencing an exciting flight of ideas, patients with mixed features have uncomfortable racing thoughts—usually depressive and anxious thoughts—that they desperately want to turn off (see the Depression With Mixed Features: Diagnostic Tips table on page 2).

Treatment recommendations

Recently, guidelines have been published for the treatment of depression with mixed features (Stahl SM et al, *CNS Spectr* 2017;22(2):203–219). Because essentially all the authors of these guidelines have financial relationships with pharmaceutical companies, we should

take these recommendations with a grain of skepticism. Nonetheless, the article presents a good overview of the current research in the field, and the treatment recommendations are not unreasonable.

The authors recommend atypical antipsychotics as first-line treatments (specifically aripiprazole, asenapine, lurasidone, quetiapine, and ziprasidone). Second-line antipsychotics include cariprazine and olanzapine/fluoxetine combination (ie, Symbyax). Traditional mood stabilizers (lithium and the anticonvulsants) are second-line, and antidepressants are relegated to third-line therapies (even in unipolar patients with mixed depression)

and only recommended in conjunction with mood stabilizers.

In actual practice, most patients are already on an antidepressant when their mixed features are discovered. The first step in such cases is to determine if the antidepressant is clearly helping the depression or contributing to the manic symptoms. If the antidepressant is helping, my policy is to leave it be and to monitor the patient closely. But if the antidepressant is aggravating manic symptoms, such as racing thoughts and insomnia, I will taper quickly over 1–2 weeks. Sometimes the antidepressant is simply ineffective, in which case I will usually taper it off, but more slowly (over 1–2 months).

In terms of antipsychotics, I am not nearly as enthusiastic about their use as the authors of the mixed depression guidelines. Although I acknowledge that some atypicals are “cleaner” than others in terms of side effects, I am concerned about the long-term risks of metabolic syndrome and tardive dyskinesia (the 1-year incidence of tardive dyskinesia on atypicals is estimated at 7%). Because of these concerns, I usually reserve atypicals for acute episodes and use traditional mood stabilizers, particularly lithium and lamotrigine, for long-term prevention. Lamotrigine is free of long-term risks; lithium, on the other hand, can cause a variety of problems such as hypothyroidism, weight gain, and (rarely) renal insufficiency. But with close monitoring, such problems can be minimized, and lithium has the extra added benefit of a clear antisuicide effect.

Psychotherapy should be considered for all cases of mixed depression. For all patients, whether in therapy or not, I emphasize a few lifestyle changes to help stabilize manic symptoms. Foremost is developing regular routines around sleep and waking. In the morning, patients should rise briskly out of bed (a dawn simulator can help) and start their day with an engaging activity. The evening routine should conjure sleep, with a relaxing activity, low lights, and an “electronics-free zone” in the half-hour before bed. Dark therapy, in which patients wear a \$10 pair of blue-light filtering glasses in the evening and sleep in pitch darkness, is a new technique for mania that has shown promise in a small controlled trial of hospitalized patients.

Recommended Treatment Options for Depression in Patients on the Bipolar Spectrum

	Name	Pearls
No Risk of Mania	Lamotrigine (50–200 mg daily)	Treats bipolar depression, but failed trials in unipolar.
	Lithium (serum levels 0.4–0.6 for depression, 0.8–1.2 for mania)	Treats bipolar depression as monotherapy; augments antidepressants in unipolar depression.
	Atypical antipsychotics (dose in low range)	For bipolar depression: cariprazine, lurasidone, olanzapine/fluoxetine combination, quetiapine. For unipolar depression (as antidepressant augmentation): aripiprazole, brexpiprazole, cariprazine, lurasidone, olanzapine/fluoxetine combination, quetiapine, risperidone, ziprasidone.
	Omega-3 fatty acids (1000–3000 mg range)	Moderate effect size for unipolar and bipolar depression, but only when EPA ≥ 1.5 times the DHA amount.
	N-acetylcysteine (2,000 mg daily)	Treats subsyndromal bipolar (but not unipolar) depression. May take 6 months to see benefits, but those benefits go away within a week of discontinuation.
	Ramelteon (8 mg qhs)	Nightly dosing of this non-sedating hypnotic reduced the frequency of bipolar depression in two small trials.
Low Risk of Mania	Pramipexole (0.75–2 mg qhs)	Effective for unipolar, bipolar, and treatment-resistant depression in 5 small controlled trials. Lacks weight gain, cognitive, or sexual side effects. Rarely, causes compulsivity syndromes (eg, gambling) and, at higher doses, mild hallucinations.
	Modafinil (up to 200 mg qam) and armodafinil (up to 250 mg qam)	Treats residual fatigue in unipolar depression and both mood and fatigue in bipolar depression. Though efficacy studies have mixed results, patients appreciate these options as they tend to improve cognition and overall functioning.
	Bupropion (150–450 mg range)	The risk of antidepressant-induced mania, from low to high, is: bupropion < SSRIs < SNRIs < tricyclics. Start bupropion low (75 mg), raise slowly (by 75 mg/week), and use with a mood stabilizer to reduce the risk further.
	Light therapy	Large effect size for bipolar and unipolar depression. To reduce risk of mania, use at midday (12 pm–2 pm), start at 15 min/day, and raise by 15 min/week to a target time of 1 hour/day. Check cet.org for effective products (eg, Carex brand).
	ECT and TMS	ECT is effective in treatment-resistant bipolar and unipolar depression with a larger effect size than TMS. Studies of TMS in bipolar depression are promising but preliminary.

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Expert Interview

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DSM-II from 1968, it defines manic-depressive illness as “a single disorder of mood, either extreme depression or elation, that dominates the mental life of the patient.”

TCPR: That’s very true. So what else did we learn from Kraepelin?

Dr. Aiken: Kraepelin did try to split the extremes of mania and depression into different illnesses, but he could not arrive at a satisfactory way of doing so because he saw so much overlap between them, particularly through mixed states. He had a keen eye for these mercurial states, noticing how his depressed patients often had various symptoms of “excitation,” even if they never had pure mania. He even complained that his contemporaries were more interested in the “pure forms” than they were in the mixed states. When a lot of research is done on the pure forms of all psychiatric disorders, I think we can hear that kind of controversy today. But practicing psychiatrists tend to see patients with a mix of many features that fit into different categories. That can make it difficult to translate the results of clinical trials into the real world of the patients who show up in our office (Kennedy-Martin T et al, *Trials* 2015;16:495).

TCPR: Then what happened with DSM-III?

Dr. Aiken: DSM-III completely split manic depression into the unipolar and bipolar sides. This wasn’t done rashly; it was based on 20 years of research showing that the extreme ends of the disorders differ in their family histories, treatment response, and course of illness. DSM-III took a categorical approach to mood disorders—but that isn’t necessarily incompatible with a dimensional approach. I think it makes sense to most people to say that, at the distal ends, depression and bipolar disorder are very different illnesses and need different treatment. You wouldn’t give a bipolar I manic an antidepressant, and you wouldn’t give a pure dysthymic Depakote, but in between there’s an overlap.

TCPR: Certainly I was trained with the conception that bipolar disorder is its own category, and to some extent, that’s still how I practice. But I’m noticing more articles in the literature about the different “flavors” of bipolar. And in DSM-5 there are so many diagnostic choices: manic episodes, manic with mixed features, hypomanic episodes, depressive with mixed features, depressive episodes. These categories do sound like they probably have more fidelity to the actual patients that I see, but on the other hand, it becomes confusing and hard to reliably diagnose patients when we have so many labels to choose from.

Dr. Aiken: I fully agree, and with DSM-5, as you pointed out, there are so many categories that, if you line them all up, they almost look like a spectrum—particularly if you include “recurrent depression with brief hypomanias,” which is listed in the appendix and refers to people with hypomanias that last less than 4 days.

TCPR: What is the definition of this new mixed features category?

Dr. Aiken: DSM-5 defines depression with mixed features as a patient who meets criteria for depression and who also has “at least 3 manic symptoms during a depression.” A quarter of unipolar depressives have mixed features by that definition, but the actual rate falls 2- to 3-fold because of a controversial decision that the DSM-5 committee made to exclude from the diagnosis symptoms of irritability, distractibility, and agitation. Either way, trying to appreciate mixed states from the separate manic and depressive criteria is like trying to visualize green by looking at yellow and blue. The original description by Koukopoulos, one of the founders of the concept, captures it much better: “The patient complains of anxiety, inner tension, irritability, anger, despair, suicidal impulses, crowded or racing thoughts, rumination, and insomnia.” (Koukopoulos A et al, *Encephale* 1992;1(1):19–21). They are “tired and wired”—driven to do something, but they don’t know what to do.

TCPR: For me, that sounds like it could describe any number of my patients who I would normally diagnose with severe depression. How would I differentiate mixed depression from severe depression with anxious features?

Dr. Aiken: Yes, it’s a difficult diagnosis to make. One clue is exactly what you said—severity. Mixed states are more severe. They have the highest rate of suicide of any bipolar condition. With higher rates of side effects and lower rates of response, treatment is difficult. The interview is colored with desperation. These patients want you to do something *now*, whereas most depressed patients have a sense of hopelessness and must be convinced that you can even do anything to help. Last week, I saw someone in a mixed state. I suggested that she try blue-light filtering glasses to help her manic symptoms. She immediately said, “I’ll go out and buy 10 of them!” That’s not what depressed people say. They say, “Yeah, that’s not gonna work. Nice try, doc.” They’re more negative and hopeless, whereas those with mixed features are impulsive and seek quick relief, such as with benzos, substance abuse, self-cutting—which can release endogenous opioids—and, in the worst cases, suicide. Even if it’s disorganized, the impulsivity of mania tends to be pleasurable or productive. In mixed states, that impulsivity is destructive.

TCPR: So it sounds like, if you see a lot of these patients, you can start to more easily recognize mixed features. That’s a result of repetition and practice. But I know there are also evidence-based guidelines and scales to help those of us who have less experience with these patients. Can you tell us about these?

Dr. Aiken: Yes, the symptoms are hard to pin down. They shift rapidly and cross into other diagnostic categories such as ADHD, PTSD, GAD, and Cluster B personality disorders. A new treatment guideline by Stahl and colleagues

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“The Bipolarity Index has a very high sensitivity as well as specificity for bipolar disorder—it also helps by identifying patients who endorse symptoms of mania but may not have a true bipolar diagnosis, which is a common problem in conditions such as ADHD, PTSD, and borderline personality disorder.”

Chris Aiken, MD

Expert Interview

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recommends taking a “probabilistic approach” to diagnosis that relies on both signs and symptoms. The Bipolarity Index is a tool that lets you rate signs of the illness on a 100-point scale (for a PDF version of the Bipolarity Index that we’ve developed for this issue, see <http://www.thecarlatreport.com/BipolarityIndex>). The index lists 5 main features that increase the probability that a patient has some form of bipolar disorder: episode characteristics, age of onset, course of illness, family history, and treatment response (Stahl SM et al, *CNS Spectr* 2017;22(2):203–219).

TCPR: How was this index developed? What data was it based on?

Dr. Aiken: The index was developed by a consensus of experts led by Gary Sachs at Massachusetts General. They gathered features that were associated with bipolar disorder, or with conversion from unipolar to bipolar, from large epidemiologic studies. Those insights have held up as the research has grown, most recently with the international BRIDGE study that looked at bipolar features in over 8,000 patients. Involving 3,305 patients, the Bipolarity Index itself has been validated in 4 studies across 4 continents. It has a very high sensitivity as well as specificity for bipolar disorder—both in the 0.9 range—which means it doesn’t expand the bipolar diagnosis; it also helps to rein it in by identifying patients who endorse symptoms of mania but may not have a true bipolar diagnosis. That’s a common problem in conditions such as ADHD, PTSD, and borderline personality disorder.

TCPR: Can we dig down a little into some of the Bipolarity Index items? Maybe you could help us understand some of the more high-yield items and how to ask about them. For example, let’s look at age of onset. How does age of onset have anything to do with the possibility of bipolar disorder?

Dr. Aiken: In bipolar, the average age of onset is 15 to 20, and in unipolar it’s 30 to 40 (Sadock BJ. *Kaplan & Sadock’s Comprehensive Textbook of Psychiatry*, 9th ed. Philadelphia, PA: Wolters Kluwer Health/Lippincott Williams & Wilkins; 2009). That’s a high-yield item that can easily be gathered by asking clients how old they were when their depression or their other manic symptoms (described in clients’ own words) began.

TCPR: Give us some of the other robust associations.

Dr. Aiken: If I had to choose 3 questions to ask in a quick interview, I would ask about age of onset, family history, and response to medications. In terms of family history, the way I often phrase the question is, “Was anyone in your family diagnosed with bipolar disorder, or did anyone have depression but also problems with anger, impulsivity, or other out-of-control behaviors?” In terms of medication response, I’ll ask, “Have you ever taken an antidepressant that made you feel much worse—agitated, irritable, anxious, wired, unable to sleep, or just more depressed?” It’s important to rule out side effects there, but it’s also important to understand that antidepressants are more likely to cause mixed states than pure manias—and for most patients, that just feels like a more severe depression. If the responses to all 3 of these questions were positive, and the patient had recurrent depression, I’d be strongly suspicious of a bipolar diathesis.

TCPR: Let’s drill down a bit into the medication response item. I’ll often get a medication history from someone and hear that the patient didn’t respond to several antidepressants, and usually my conclusion is treatment-resistant depression rather than bipolar disorder.

Dr. Aiken: Right, there are many reasons why a patient may not respond to antidepressants, and bipolar is just one of them, so by itself that would only add 5 points to the patient’s score on the index. It takes a score of at least 50 to indicate a strong probability of bipolar disorder.

TCPR: Thank you for your time, Dr. Aiken.



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Cyclothymia with bipolar II

Typical patient statement

“My moods are all over the place. I don’t know what normal is. I hide it well—I can seem like the life of the party, but it’s really just an act. I have waves of anxiety, but other times I’m wide open. I’m usually great on a job when I first start—I’m full-throttle and get it all done—but after a few months, I burn out and can’t concentrate.”

Diagnostic tips

Around 40% of patients with bipolar II disorder have an underlying cyclothymic temperament. These patients have a stormier course than their classic bipolar II

counterparts, who have productive, euphoric hypomanias and long periods of stable mood. In contrast, cyclothymic mood swings start early in life and are woven into patients’ temperament, allowing little time for a stable identity to develop. Euphoria is rare in these patients, and mixed states are common, with all the despairing, paradoxical symptoms described in the Diagnostic Tips table on page 2.

These patients have high rates of comorbidities, particularly borderline personality disorder, addictions, anxiety disorders, PTSD, OCD, ADHD, and eating disorders. Detecting bipolar symptoms amidst all these comorbidities is difficult,

so the Bipolarity Index is particularly useful in this group; in one study, it outperformed other screening tools at distinguishing bipolar disorder from pure forms of Cluster B personality disorders. (Ed note: For more information on the Bipolarity Index, see this issue’s QA interview with Dr. Aiken).

Treatment

Psychotherapy should be part of the treatment for this group. Dialectical behavior therapy is often helpful, and it blends well with bipolar-specific therapies, which emphasize regular daily routines.

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Research Updates IN PSYCHIATRY

SCHIZOPHRENIA

Estrogen Modulator Raloxifene Not Helpful for Schizophrenic Women

REVIEW OF: Weiser M et al, *J Clin Psychiatry* 2017;78:e758–e765

Since estrogen can affect neurotransmitter functioning, there has been some interest in using estrogen modulators to treat psychiatric conditions, including schizophrenia. Raloxifene is a selective estrogen receptor modulator (SERM) with some preliminary evidence for effectiveness in women with schizophrenia.

In this double-blind, multi-center study, 200 postmenopausal schizophrenic/schizoaffective women were

treated for 16 weeks with either raloxifene or placebo augmentation of their antipsychotic drug treatment regimen. The study was conducted at 38 sites in Romania and Moldova, suggesting an average of 5 patients per site. The results were unequivocally negative. Indeed, subjects in the raloxifene treatment group fared significantly worse on the Positive and Negative Syndrome Scale (PANSS) than did the placebo group, an unexpected outcome the authors attribute to chance. There were no significant differences between groups in Clinical Global Impression—Severity or Composite Brief Assessment of Cognition in Schizophrenia scores.

TCPR'S TAKE

As the authors indicate, their data “does

not support the use of raloxifene in severely decompensated schizophrenia patients.” These results are clear, but they may not be definitive. Given the many research sites, the potential for inter-site variability (in diagnosis, conduct of the study, assessments, etc) was quite large. In addition, the postmenopausal schizophrenic women had been ill for an average of over 20 years and had an average of about 20 hospitalizations, suggesting they were refractory to conventional treatments. There is a need for additional studies, with more subjects per site, less-ill women, and perhaps different SERMs.

—Robert T. Rubin, MD

Dr. Rubin has disclosed that he has no relevant financial or other interests in any commercial companies pertaining to this educational activity.



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In terms of pharmacotherapy, it's best to stabilize the bipolar disorder before treating the comorbidities, though this is a challenge as patients usually request treatment for the comorbidities first. Lamotrigine has the best evidence for cyclothymic disorder and is conveniently effective for borderline personality disorder as well. Many treatments for the comorbidities that are common in this group can destabilize mood, such as antidepressants and stimulants, but there are many that don't. Below are some options with low risk of mood destabilization. Each is supported by at least one randomized controlled trial, and I've starred my top choice(s) in each category:

- ADHD: clonidine*, guanfacine, modafinil/armodafinil*
- Borderline personality disorder: lamotrigine* and other anticonvulsants, atypical antipsychotics, and omega-3 fatty acids
- OCD: lamotrigine*, ondansetron, topiramate, memantine, and atypical antipsychotics
- Anxiety: gabapentin*, pregabalin, clonidine, and propranolol, as well as complementary and alternative medicine therapies: silexan (lavender extract)*, chamomile, and probiotics

Depression with short-duration hypomania

Typical patient statement

Psychiatrist: “When you think about those elevated states—hyped up, sleeping less, talkative, irritable, or a bit impulsive—what's the longest they've lasted?”

Patient: “Just a few hours.”

Psychiatrist: “I understand each of those symptoms can be brief and shift rapidly, but think carefully: have you ever been ‘that way’ for at least 4 days?”

Patient: “No, I'd say no more than 2–3 days.”

Diagnostic tips

Many patients with recurrent depression endorse clear hypomanic states that are just short of the 4-day duration required in the DSM, and these short-duration hypomanias are included in DSM-5 as a “condition for further study.” They are particularly common in adolescents who go on to develop full bipolar disorder, but short-duration hypomania can persist throughout life, and studies suggest that such cases represent an “intermediate phenotype” between unipolar and bipolar.

Treatment

One study supports lamotrigine for these

patients, and this agent seems particularly effective in patients with quick, brief mood swings (McCraw S and Parker G, *J Psychopharmacol* 2016;30(6):554–558).

Antidepressants should be used with caution, though they are less risky here than they are in full bipolar disorder. In general, the more recent, more severe, and more frequent the manic symptoms, the greater the risks with antidepressants.

No mania vs. long-forgotten mania

Typical patient statement

“I'm not at all like my father—he had bipolar. I'm just depressed, but antidepressants never helped. I used a lot of drugs in my teens and 20s, but I've been sober now 30 years, and depressed for nearly all of them.”

Diagnostic tips

As you use the Bipolarity Index, you will encounter patients who deny manic symptoms but have multiple signs of bipolarity. These patients usually have recurrent depression and score in the 40–60 range on the Bipolarity Index. This is likely a mixed group including: 1) true unipolar depression; 2) older patients, who have forgotten their manias (pure mania is

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CME Post-Test

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Below are the questions for this month's CME/CE post-test. This page is intended as a study guide. Please complete the test online at www.TheCarlatReport.com. Note: Learning Objectives are listed on page 1.

- What is the estimated prevalence of bipolar spectrum among depressed patients (including depressed patients with short-duration hypomania)? (LO #1)

<input type="checkbox"/> a. 10%–20%	<input type="checkbox"/> c. 30%–40%
<input type="checkbox"/> b. 20%–30%	<input type="checkbox"/> d. 40%–50%
- According to the Bipolarity Index, which of the following features does not increase the probability that a patient has some form of bipolar disorder? (LO #2)

<input type="checkbox"/> a. Treatment response	<input type="checkbox"/> c. Family history
<input type="checkbox"/> b. Environmental factors	<input type="checkbox"/> d. Age of onset
- The severity of early, prodromal symptoms of bipolar disorder can help identify high-risk patients under age 25. (LO #1)

<input type="checkbox"/> a. True	<input type="checkbox"/> b. False
----------------------------------	-----------------------------------
- According to Dr. Aiken, which of the following is characteristic of a patient with mixed features in bipolar disorder? (LO #2)

<input type="checkbox"/> a. Emotional blunting	<input type="checkbox"/> c. Impulsivity
<input type="checkbox"/> b. Feelings of detachment or unreality	<input type="checkbox"/> d. Hallucinations
- In a recent study on raloxifene in women with schizophrenia, patients in the raloxifene treatment group fared only slightly better on the Positive and Negative Syndrome Scale (PANSS) than those in the placebo group. (LO #3)

<input type="checkbox"/> a. True	<input type="checkbox"/> b. False
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The Bipolar Spectrum: Practical Tips for Diagnosis and Treatment

Continued from page 6

more prominent in young adulthood); and 3) younger patients, who are at high risk of conversion to bipolar disorder (see next section).

Treatment

There is not a clear treatment for these patients, but there is a definite need to watch carefully (particularly with antidepressants) and gather more information. Outside of antidepressants, I look for treatments that work in both unipolar and bipolar depression (see Recommended Treatment Options table on page 3).

The bipolar prodrome

Typical patient statement

"I have bipolar disorder, and I'm worried about my teenage son. He's moody,

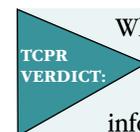
depressed, and argumentative. He smokes a lot of weed and doesn't care about his schoolwork. We've been to different doctors and they've diagnosed depression, social anxiety, and ADHD. The treatments seem to work at first, but they always wear off."

Diagnostic tips

Bipolar is a highly genetic illness, and research is starting to identify the early, prodromal signs of the disorder. Those at highest risk are patients under age 25 who present with significant psychiatric symptoms and have a first-degree relative with bipolar disorder. It is the severity of the presenting symptoms that indicates the risk, rather than the type, as prodromal bipolarity can present as anxiety, ADHD, substance abuse, and nonspecific behavioral problems.

Treatment

Family therapy, which aims to improve communication and reduce levels of expressed emotion, has the best research support and is a first-line recommendation in a new treatment algorithm for prodromal bipolar disorder. In that algorithm, medications are only used if symptoms interfere with functioning, and antidepressants are not allowed if subsyndromal manic symptoms are present (if they are, mood stabilizers are used). Studies also support omega-3 fatty acids in this group.



When evaluating depression, keep the bipolar spectrum in mind. Treatment informed by this approach might be more effective.

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This Month's Focus:
Bipolar Disorder

**Next month in *The Carlat Psychiatry Report*:
Couples and Family Therapy**

Note From the Editor-in-Chief

When I was training in the 1990s, diagnosing bipolar disorder seemed straightforward. These patients often came to our attention because of a flagrant manic episode. You may still remember the first time you treated a manic patient—I certainly do. He was a man in his 20s with flowing red hair and a messianic beard, who was admitted after police found him doing cartwheels on the highway during rush hour. He told me, in an ebullient rush of language, that he was Jesus Christ and therefore invincible—as “proven” by the fact he’d survived his highway stunt.

Seeing such patients may have given us the impression of a clear distinction between those who experience depressive episodes interspersed with mania, and those who are just depressed. But over time, that distinction has become less clear. In this issue, Dr. Chris Aiken describes the many variations of presentations that land on the “bipolar spectrum,” including bipolar I and II, cyclothymia, depression with mixed features, depression with short-duration hypomania ... and so on. Dr. Aiken has no agenda and is hardly advocating that anyone with a whiff of bipolar disorder must be put on lithium or atypical antipsychotics. But he reminds us that mood disorders lie on a continuum and that making categorical distinctions is often not helpful. His is a thoughtful approach and one that I hope you’ll find useful in your practice.

Best, Danny
dcarlat@thecarlatreport.com



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