

ADHD

An artistic illustration of a human head in profile, facing right. The head is rendered in a light, textured beige color. A large, dark brown silhouette of a person is climbing a blue ladder that extends from the bottom left towards the top of the head. The background is a solid dark brown color. In the upper right, the letters 'ADHD' are written in a large, bold, dark brown font with a white outline. To the right of the head, there are several concentric, dashed black circles. The overall style is graphic and symbolic.

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Adults with ADHD and bipolar disorder often have comorbid agoraphobia, posttraumatic stress disorder, social phobia, or alcohol or drug addiction.



Meeting of the Minds

Ask Dr. Ghaemi about comorbid adult ADHD and bipolar disorder
For details, see page 52

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Only half the diagnosis in an adult with inattention?

Overlapping symptoms may obscure comorbid bipolar illness

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An adult with function-impairing inattention could have attention-deficit/hyperactivity disorder (ADHD), bipolar disorder (BD), or both. Comorbid ADHD and BD often is unrecognized, however, because patients are more likely to report ADHD-related symptoms than manic symptoms.¹

To help you recognize comorbid ADHD/BD—and protect adults who might switch into mania if given stimulants or antidepressants—this article describes a hierarchy to diagnose and treat this comorbidity. Based on the evidence and our experience, we:

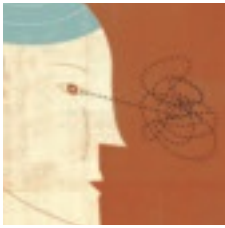
- discuss how to differentiate between these disorders with overlapping symptoms
- provide tools and suggestions to screen for BD and adult ADHD
- offer 3 algorithms to guide your diagnosis and choice of medications.

Clinical challenges

Prevalence is unclear. Adult ADHD—with an estimated prevalence of 4.4%²—is more common than BD. Lifetime prevalences of BD types I and II are 1.6% and 0.5%, respectively.³ Studies of ADHD/BD comorbidity suggest wide-ranging prevalence rates:

- 9% to 21% of BD patients may have adult ADHD^{2,4,5}
- 5% to 47% of adult ADHD patients may have BD.^{2,6-8}

continued



Adult ADHD/BD

Clinical Point

Shared diagnostic criteria include talkativeness, distractibility, increased physical activity, and loss of social inhibitions

Table 1

Overlap between DSM-IV-TR diagnostic criteria for ADHD and bipolar mania

Overlapping symptoms

ADHD	Bipolar mania
Talks excessively	More talkative than usual
Easily distracted/jumps from one activity to the next	Distractibility or constant changes in activity or plans
Fidgets Difficulty remaining seated Runs or climbs about inappropriately Difficulty playing quietly On the go as if driven by a motor	Increased activity or physical restlessness
Interrupts or butts in uninited Blurts out answers	Loss of normal social inhibitions

Nonoverlapping symptoms

ADHD
Forgetful in daily activities Difficulty awaiting turn Difficulty organizing self Loses things Avoids sustained mental effort Does not seem to listen Difficulty following through on instructions/fails to finish work Difficulty sustaining attention Fails to give close attention to details/makes careless mistakes
Bipolar mania
Inflated self-esteem/grandiosity Increase in goal-directed activity Flight of ideas Decreased need for sleep Excessive involvement in pleasurable activities with disregard for potential adverse consequences Marked sexual energy or sexual indiscretions
ADHD: attention-deficit/hyperactivity disorder
Source: Adapted and reprinted with permission from reference 12

Underdiagnosis. Adult ADHD/BD is a more severe illness than ADHD or BD alone and is highly comorbid with agoraphobia, social phobia, posttraumatic stress disorder, and alcohol or drug addiction. Adults with ADHD/BD have more frequent affective episodes, suicide attempts, violence, and legal problems.⁴ Diagnosing this comorbidity remains a challenge, however, because:

- identifying which symptoms are caused by which disorder can be difficult
- BD tends to be underdiagnosed⁹
- patients often misidentify, underreport, or deny manic symptoms^{1,10,11}
- if a patient presents with active bipolar symptoms, DSM-IV-TR criteria require

that ADHD not be diagnosed until mood symptoms are resolved.

Overlapping symptoms. ADHD and bipolar mania share some DSM-IV-TR diagnostic criteria, including talkativeness, distractibility, increased activity or physical restlessness, and loss of social inhibitions (*Table 1*).¹² Overlapping symptoms also are notable within ADHD diagnostic criteria (*Table 2, page 51*). In the inattention category, for example, “easily distracted by extraneous stimuli,” “difficulty sustaining attention in tasks,” and “fails to give close attention to details” are considered 3 separate symptoms. In the hyperactivity category, “often leaves seat,” “often runs

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Table 2

DSM-IV-TR diagnostic criteria for attention-deficit/hyperactivity disorder

Inattention

≥6 symptoms have persisted ≥6 months to a degree that is maladaptive and inconsistent with developmental level.

The patient often:

- fails to give close attention to details or makes careless mistakes
- has difficulty sustaining attention in tasks
- does not seem to listen when spoken to directly
- does not seem to follow through on instructions and fails to finish work
- has difficulty organizing tasks
- avoids tasks that require sustained mental effort
- loses things necessary for activities
- is easily distracted
- is forgetful in daily activities

Hyperactivity/impulsivity

≥6 symptoms have persisted ≥6 months to a degree that is maladaptive and inconsistent with developmental level.

The patient often:

- fidgets
- leaves seat
- shows excessive movement or feels internal restlessness
- has difficulty engaging quietly in leisure activities
- is “on the go” or often acts as if “driven by a motor”
- talks excessively
- blurts out answers before questions have been completed
- has difficulty awaiting turn
- interrupts or intrudes on others (such as butts into conversations or games)

Diagnosis requires evidence of inattention or hyperactivity/impulsivity or both

Some hyperactive/impulsive or inattentive symptoms that caused impairment were present before age 7

Some impairment from symptoms is present in ≥2 settings (such as at school, work, or home)

Symptoms do not occur exclusively during the course of a pervasive developmental disorder, schizophrenia, or other psychotic disorder and are not better accounted for by another mental disorder (mood disorder, anxiety disorder, dissociative disorder, or a personality disorder)

Source: DSM-IV-TR

about or climbs excessively,” and “often on the go, or often acts as if driven by a motor” are 3 separate symptoms.

Given ADHD’s relatively loose diagnostic criteria and high comorbidity in adults with mood disorders, the question of whether adult ADHD/BD represents comorbidity or diagnostic overlap remains unresolved. For the clinician, the disorders’ nonoverlapping features (*Table 1, page 48*) can assist with the differential diagnosis. For example:

- ADHD symptoms tend to be chronic and BD symptoms episodic.
- ADHD patients may have high energy but lack increased productivity seen in BD patients.
- ADHD patients do not need less sleep or have inflated self-esteem like symptomatic BD patients.
- Psychotic symptoms such as hallucinations or delusions might be present in severe BD but are absent in ADHD.

Mood symptoms first

A diagnostic hierarchy is implicit in DSM-IV-TR; anxiety disorders are not diagnosed during an active major depressive or manic episode, and schizophrenia is not diagnosed on the basis of psychotic symptoms during an active major depressive or manic episode. Mood disorders sit atop this implied diagnostic hierarchy and must be ruled out before psychotic or anxiety disorders are diagnosed. Similarly, most personality disorders are not diagnosed during an active mood or psychotic episode.

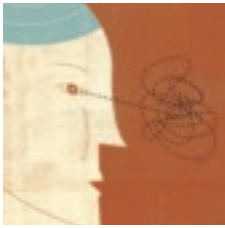
Diagnosing adult ADHD when a patient is actively depressed or manic is inconsistent with this hierarchy and conflicts with extensive nosologic literature.¹³ We suggest that ADHD—a cognitive-behavioral problem—not be diagnosed solely on symptoms observed when a patient is experiencing a mood episode or psychotic illness.

Bipolar disorder. Two useful mnemonics (*Table 3, page 52*) assist in screening for DSM-IV-TR symptoms of BD type I:

- Pure mania consists of euphoric mood and ≥3 of 7 DIGFAST criteria, or irritable mood and ≥4 of 7 DIGFAST criteria

Clinical Point

ADHD patients do not need less sleep or have increased productivity or inflated self-esteem like symptomatic BD patients



Adult ADHD/BD

Clinical Point

Inattentiveness in adult ADHD may manifest as neglect, poor time management, motivational deficits, or forgetfulness

Table 3

Mnemonics for diagnostic symptoms of pure and mixed bipolar mania

DIGFAST* for bipolar mania symptoms **SIGECAPS† bipolar depression symptoms**

D istractibility	S leep
I nsomnia	I nterest
G randiosity	G uilt
F light of ideas	E nergy
A ctivities	C oncentration
S peech	A ppetite
T houghtlessness	P sychomotor
	S uicide

Pure mania: Euphoric mood with ≥ 3 DIGFAST criteria or irritable mood with ≥ 4 DIGFAST criteria.

Mixed mania: Depressed mood with ≥ 4 DIGFAST criteria and ≥ 4 SIGECAPS criteria.

* Developed by William Falk, MD

† Developed by Carey Gross, MD

Source: Adapted from Ghaemi SN. *Mood disorders*. New York: Lippincott; 2003

- Mixed mania consists of depressed mood with ≥ 4 of 7 DIGFAST criteria and ≥ 4 of 8 SIGECAPS criteria.

To be diagnostic, these symptoms must cause substantial social or occupational

dysfunction and be present at least 1 week. Diagnose BD type I if a patient has experienced a single pure or mixed manic episode at any time, unless the episode had a medical cause such as hyperthyroidism or antidepressant use. Because patients with mixed episodes experience depressed mood, assess any patient with clinical depression for manic symptoms. Otherwise, a patient with a mixed episode could be misdiagnosed as having unipolar depression instead of BD type I.¹⁴

BD type II also has been observed in patients with comorbid adult ADHD/BD.^{4,6} The main difference between BD types I and II is that manic symptoms in type II are not severe enough to cause functional impairment or psychotic symptoms.¹⁵

Adult ADHD. The clinical interview seeking evidence of inattention and hyperactivity/impulsivity remains the basis of adult ADHD diagnosis (*Table 2, page 51*). Key areas are:

- the patient's past and current functional impairment
- whether substantial impairment occurs in at least 2 areas of life (such as school, work, or home).

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Adult ADHD: Only half the diagnosis?



S. Nassir Ghaemi, MD, MPH

Associate Professor of Psychiatry and Public Health
Emory University, Atlanta, GA

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Interactive Q-and-A to follow

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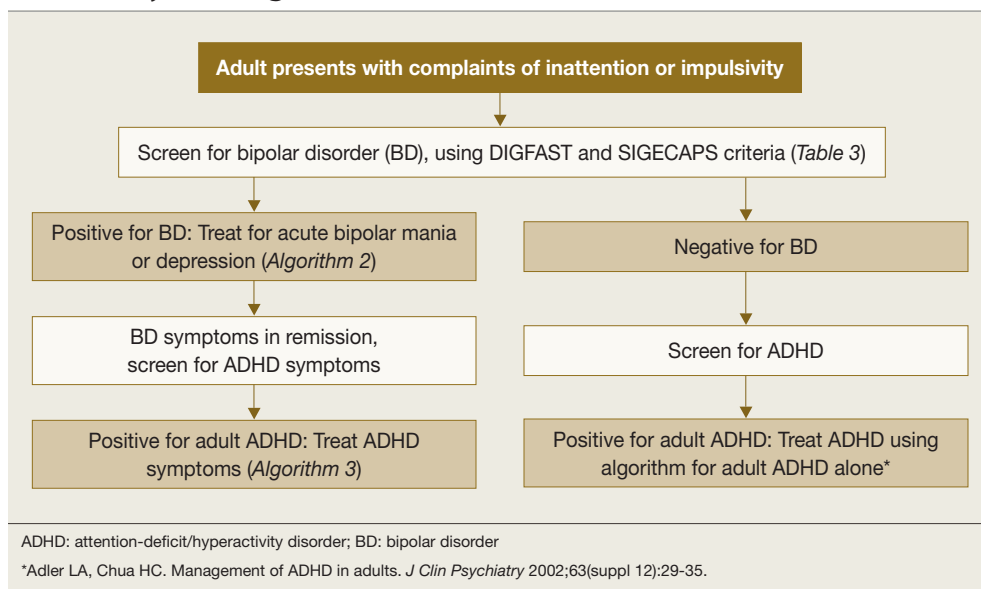
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Hierarchy for diagnosis and treatment of adult ADHD/BD



Take medical, educational, social, psychological, and vocational histories, and rule out other conditions before concluding that adult ADHD is the appropriate diagnosis.¹⁶ In adult ADHD, inattentive symptoms become far more prominent, about twice as common as hyperactive symptoms.¹⁷ Inattentive symptoms may manifest as neglect, poor time management, motivational deficits, or poor concentration that results in forgetfulness, distractibility, item misplacement, or excessive mistakes in paperwork.¹⁸ When impulsive symptoms persist in adults, they may manifest as automobile accidents or low tolerance for frustration, which may lead to frequent job changes and unstable, interrupted interpersonal relationships.¹⁸

Neuropsychological testing is not required to make an adult ADHD diagnosis but can help establish the breadth of symptoms or comorbidity.¹⁷ Rating scales can screen, gather data (including presence and severity of symptoms), and measure treatment response.¹⁶ Commonly used rating scales include:

- Conners' Adult ADHD Rating Scales¹⁹
- Brown Attention Deficit Disorder Rating Scale for Adults²⁰
- Adult ADHD Self-Report Scale.²¹

When using rating scales, remember that adult psychopathology can distort

perceptions, and some self-report scales have questionable reliability.¹⁶

Treatment recommendations

Limited data. We found only 1 study on adult ADHD/BD treatment. In this open trial,²² 36 adults with comorbid ADHD and BD received bupropion SR, up to 200 mg bid, for ADHD symptoms while maintained on mood stabilizers, antipsychotics, or both. Improvement was defined as $\geq 30\%$ reduction in ADHD Symptom Checklist Scale scores, without concurrent mania. After 6 weeks, 82% of patients had improved; 1 dropped out at week 2 because of hypomanic activation. Methodologic limitations included trial design (non-randomized, nonblinded, short duration) and patient selection (90% of subjects had BD type II).

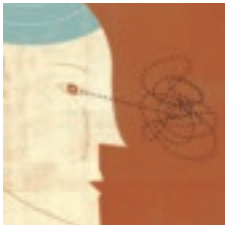
In the absence of adequate data on adult ADHD/BD, studies in children suggest:

- stimulants may not be effective for ADHD symptoms in patients with active manic or depressive symptoms
- mood stabilization is a prerequisite for successful pharmacologic treatment of ADHD in patients with both ADHD and manic or depressive symptoms.^{23,24}

Follow the hierarchy. First treat acute mood symptoms, then reevaluate and

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Impulsivity in adult ADHD may manifest as low tolerance for frustration, leading to frequent job changes or unstable relationships



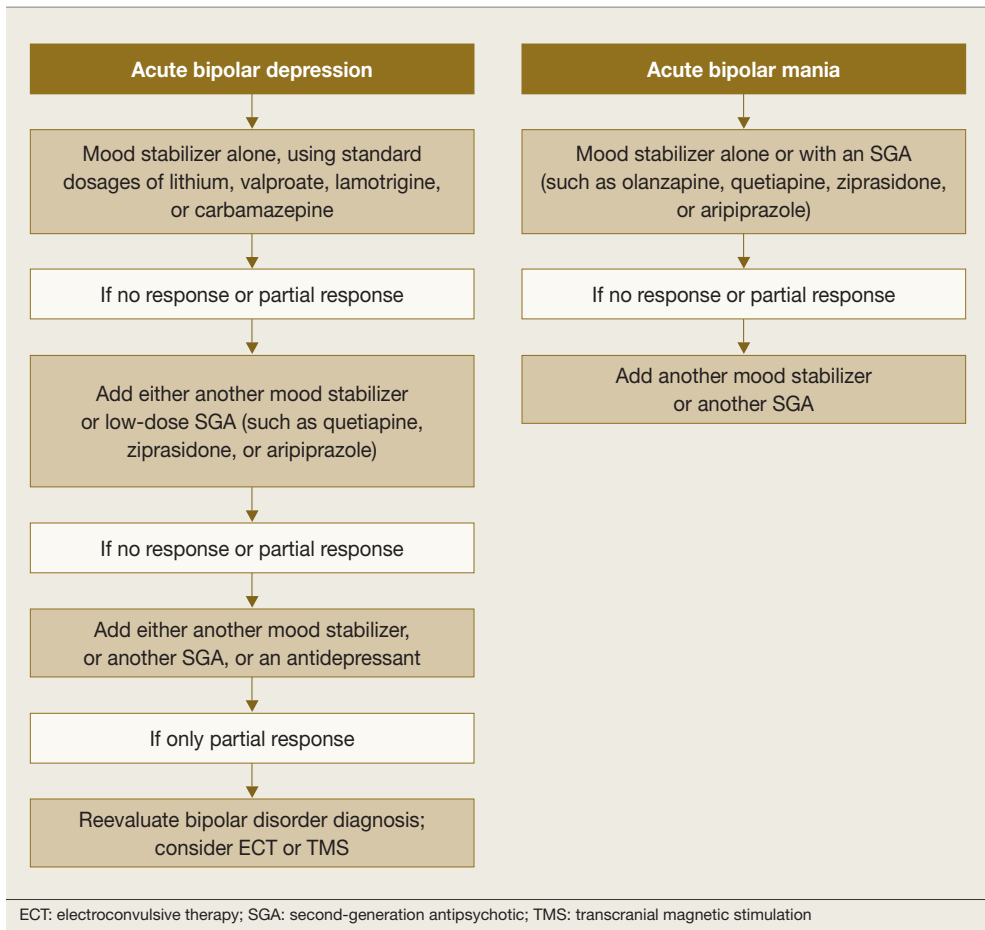
Adult ADHD/BD

Clinical Point

For acute bipolar depression, adding an antidepressant is no more effective than using a mood stabilizer alone

Algorithm 2

Treating acute episodes of bipolar disorder



possibly treat ADHD symptoms if they persist during euthymia (*Algorithm 1, page 53*). When a patient meets criteria for adult ADHD/BD, first stabilize bipolar manic or depressive symptoms (*Algorithm 2*). For acute mania, treat with standard mood stabilizers (lithium, valproate, lamotrigine, or carbamazepine) with or without a second-generation antipsychotic.²⁵ Starting stimulants for ADHD when patients have active mood symptoms is suboptimal and potentially harmful because of the risk of inducing mania. For acute bipolar depression, adjunctive antidepressant treatment has been found to be no more effective than a mood stabilizer alone.²⁶

After bipolar symptoms respond or remit, reassess for adult ADHD. If ADHD symptoms persist during euthymia, additional treatment may be indicated.

Very little evidence exists on treating adult ADHD/BD; as mentioned, bupropion

is the only medication studied in this population. For adult ADHD alone, clinical trials have shown varying efficacy with bupropion,^{27,28} atomoxetine,²⁹ venlafaxine,^{30,31} desipramine,³² methylphenidate,³³ mixed amphetamine salts,³⁴ and guanfacine.³⁵ Whether these treatments can be generalized as safe and efficacious for comorbid adult ADHD/BD is unclear. Nonetheless, we suggest using bupropion first, followed by atomoxetine or guanfacine before you consider amphetamine stimulants (*Algorithm 3, page 59*).

Reducing mania risk

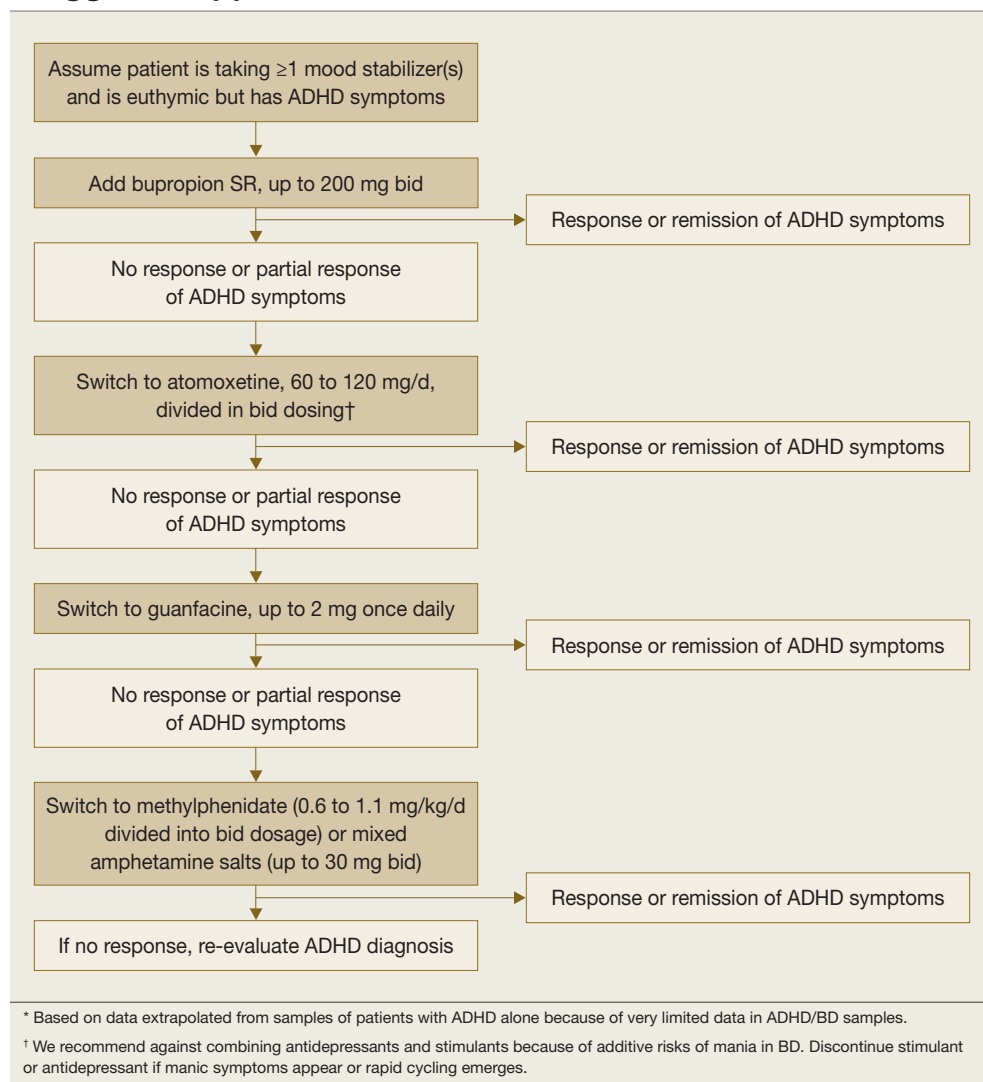
Antidepressants and stimulants may help adults with ADHD alone, but risks of mania and rapid cycling limit their use in adults with ADHD/BD.

Stimulants and mania. One study found a 17% manic switch rate when methylphenidate

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Algorithm 3

Suggested approach to adult ADHD with comorbid BD*



(≤10 mg bid) was given to 14 bipolar depressed adults (10 BD type I, 2 BD type II, and 2 with secondary mania) taking mood stabilizers.³⁶ A chart review of 82 bipolar children not taking mood stabilizers found an 18% switch rate with methylphenidate or amphetamine.³⁷ Another chart review of 80 children with BD type I found that past amphetamine treatment (but not history of ADHD diagnosis or antidepressant treatment) was associated with more severe bipolar illness.³⁸

No studies have examined predictors of amphetamine-induced mania. In our clinical experience, triggers are similar to those that can cause antidepressant-induced mania, such as:

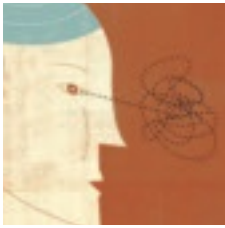
- recent manic episodes

- current rapid cycling
- past antidepressant-induced mania.

Antidepressants and mania. When 64 patients with acute bipolar depression received both antidepressants and mood stabilizers in a randomized, double-blind trial, switch rates into mania or hypomania were 10% for bupropion, 9% for sertraline, and 29% for venlafaxine.³⁹ In a meta-analysis of clinical trials using selective serotonin reuptake inhibitors (SSRIs) or tricyclic antidepressants (TCAs), the manic switch rate was three-folds higher with TCAs than SSRIs.⁴⁰ Antidepressant use in bipolar patients was associated with rapid cycling in the only randomized study of this topic.⁴¹

Clinical Point

In adult ADHD/BD, we suggest trying bupropion first, then atomoxetine or guanfacine, before you consider using stimulants



Adult ADHD/BD

Clinical Point

Adult ADHD/BD is highly comorbid with agoraphobia, social phobia, PTSD, and alcohol and drug addiction

Insufficient data exist to clarify whether mania induction with antidepressants is dose-dependent.⁴² Factors associated with antidepressant-induced mania include:

- previous antidepressant-induced mania
- family history of BD
- exposure to multiple antidepressant trials⁴²
- history of substance abuse and/or dependence.⁴³

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Related Resources

- BD information and resources. www.psycheducation.org.
- ADHD Information and resources. www.adhdnews.com.
- Phelps J. *Why am I still depressed? Recognizing and managing the ups and downs of bipolar II and soft bipolar disorder*. New York: McGraw-Hill; 2006.

Drug Brand Names

Amphetamine/ Dextroamphetamine • Adderall	Guanfacine • Tenex Lamotrigine • Lamictal Lithium • Eskalith, Lithobid Methylphenidate • Ritalin Quetiapine • Seroquel Sertraline • Zoloft
Aripiprazole • Abilify Atomoxetine • Strattera Bupropion • Wellbutrin Carbamazepine • Tegretol Desipramine • Norpramin Dextroamphetamine • Dexedrine	Valproate • Depakote Venlafaxine • Effexor Ziprasidone • Geodon

Disclosures

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Bottom Line

Screen for bipolar disorder in adults with ADHD symptoms. In those with ADHD and BD, first treat bipolar symptoms with mood stabilizers. When BD symptoms remit, reassess ADHD symptoms to determine if further treatment is indicated. If so, consider nonamphetamine agents before trying stimulants, and carefully monitor for mania or worsening BD.

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