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EXPERT PANEL SUPPLEMENT

DIFFERENTIAL DIAGNOSIS OF ADULT ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: TREATMENT OPTIONS AND COMORBIDITY CONSIDERATIONS

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ABSTRACT

Attention-deficit/hyperactivity disorder (ADHD) in adults occurs at a prevalence rate that is higher than the prevalence of many major psychiatric disorders in adults. Thus, adult patients with ADHD often present with comorbid conditions, each of which alters the course of ADHD, overall treatment recommendations, and symptom response differently. Common ADHD comorbidities include major depressive disorder (MDD), bipolar disorder, and substance use disorders. Algorithms have been developed to aid clinicians in determining which presenting disorder to treat first, and additional studies have helped elucidate which pharmacologic and non-pharmacologic treatments best treat each comorbid disorder without worsening symptoms of another.

In this Expert Panel Supplement, David Goodman, MD, discusses the prevalence and diagnostic distinctions between ADHD in adults and depression, including both MDD and dysthymia; Roger McIntyre, MD, FRCPC, reviews the phenomenology, illness progression, and treatment options for patients with ADHD and comorbid bipolar disorder; and Oscar Bukstein, MD, MPH, reviews both background and practical considerations in understanding, evaluating, and treating adults with co-existing substance use disorders and ADHD.

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Statement of Need and Purpose

Despite treatment, many adults with attention-deficit/hyperactivity disorder (ADHD) remain substantially impaired in their daily functioning and a significant public health need exists to develop better treatment interventions with a special focus on promoting competence and functional improvement. ADHD is a lifelong neurodevelopmental disorder and one of the most common psychiatric disorders both in children and adults, but is consistently underrecognized. Since conditions which are often comorbid with ADHD are also common in the general population, the ability to properly recognize ADHD and its comorbidities is required for psychiatrists and primary care physicians (PCPs) to effectively treat affected patients. As with children with ADHD, adults show functional impairments in multiple domains, often including poor educational performance, occupational problems, and relationship difficulties. The presence of comorbid conditions adds further debility across these different domains of functioning. Management of multiple medical, mental health, and psychosocial problems over time will often be ineffective if ADHD is not adequately managed.

The most effective management should be multimodal, with patients benefiting from caring professionals with special expertise in ADHD as well as the PCP. For patients with comorbidities, the PCP and mental health professional should be in close communication about treatment decisions; the mental health professional may be in the best position to recommend pharmacotherapy. The PCP has an important role in assuring preventive care and recognizing and treating acute and chronic comorbidities or medical illnesses as they develop over time. Adults' differing patterns of comorbidity and symptom heterogeneity pose new conceptual, diagnostic, and treatment challenges. Education is needed to increase the detection and treatment of comorbid adult ADHD (and its reverse comorbidity) to determine whether effective treatment would reduce the onset, persistence, and severity of disorders that co-occur with adult ADHD.

Target Audience

This activity is designed to meet the educational needs of psychiatrists.

Learning Objectives

At the completion of this activity, participants should be better able to:

- Predict challenges to diagnosing and managing comorbidities in adults with ADHD
- Assess current evidence relating to treatment efficacy for adults with ADHD and comorbid depression, bipolar disorder, and substance use disorder
- Summarize the evidence related to ADHD and substance use disorder and how to minimize misuse and diversion when treating ADHD patients

Faculty Affiliations and Disclosures

David Goodman, MD, is director of the Adult Attention Deficit Disorder Center of Maryland and Suburban Psychiatric Associates in Lutherville, and assistant professor in the Department of Psychiatry and Behavioral Sciences at Johns Hopkins School of Medicine in Maryland. Dr. Goodman is a consultant to Eli Lilly, Forest, McNeil, New River, and Shire; is on the speaker's bureaus of Forest, McNeil, Shire, and Wyeth; receives research support from Cephalon, Eli Lilly, Forest, McNeil, New River, and Shire; has received honoraria from Eli Lilly, Forest, McNeil, Shire, and Wyeth; and is an equity shareholder in Wyeth. Dr. Goodman discusses unapproved/investigational uses of bupropion for the treatment of attention-deficit/hyperactivity disorder.

Roger McIntyre, MD, FRCPC, is associate professor of psychiatry and pharmacology at the University of Toronto,

and head of the Mood Disorders Psychopharmacology Unit at the University Health Network in Toronto, Canada. Dr. McIntyre is on the advisory boards of AstraZeneca, Biovail, Bristol-Myers Squibb, Eli Lilly, GlaxoSmithKline, Janssen-Ortho, Lundbeck, Organon, Pfizer, Schering-Plough, Shire, and Solvay/Wyeth; is on the speaker's bureaus of AstraZeneca, Biovail, Eli Lilly, Janssen-Ortho, Lundbeck, and Wyeth; receives grant/research support from Eli Lilly, Janssen-Ortho, the National Alliance for Research on Schizophrenia and Depression, Shire, and the Stanley Medical Research Institute; and receives honoraria from AstraZeneca, Bristol-Myers Squibb, and Solvay/Wyeth. Dr. McIntyre discusses unapproved/investigational uses of psychostimulants for the treatment of attention-deficit/hyperactivity disorder.

Oscar Bukstein, MD, MPH, is professor of psychiatry at the Western Psychiatric Institute and Clinic at the University of Pittsburgh School of Medicine in Pennsylvania. Dr. Bukstein has received research support from Shire. Dr Bukstein discusses unapproved/investigational uses of bupropion and modafinil for the treatment of attention-deficit/hyperactivity disorder.

CME Course Director **James C.-Y. Chou, MD**, is associate professor of psychiatry at Mount Sinai School of Medicine. Dr. Chou has received honoraria from AstraZeneca, Bristol-Myers Squibb, Eli Lilly, GlaxoSmithKline, Janssen, and Pfizer.

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ADULT ADHD AND COMORBID DEPRESSIVE DISORDERS: *DIAGNOSTIC CHALLENGES AND TREATMENT OPTIONS*

David Goodman, MD

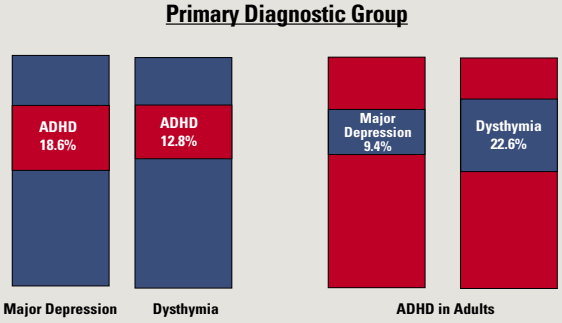
Introduction

Attention-deficit/hyperactivity disorder (ADHD) and major depressive disorder (MDD) are separately common mental health conditions that can have an adverse effect on a patient's quality of life if left untreated. These disorders frequently co-occur with one another, which can lead to increased patient suffering and diagnostic challenges for the treating clinician. In the United States adult population, epidemiological data show that the prevalence rate for MDD is 6.7%, while the ADHD prevalence rate in US adults is 4.4%.[1,2] This epidemiological data represents the general population and likely underestimates the prevalence rates in clinic or practice patients. Examining the concurrent comorbid rate, if a patient has MDD, the likelihood of that patient also having ADHD is 18.6%; if the patient has ADHD, the likelihood of that patient having comorbid MDD is 9.4%.[3-5] If the patient has dysthymia, the comorbid rate of ADHD is 12.8%, while those adults with ADHD have a comorbid rate of dysthymia of 22.6% (Slide 1).[1]

Diagnostic Distinction Between ADHD and MDD

The diagnostic distinction between ADHD and MDD is a critical aspect of clinical evaluation that often presents challenges and confusion to the treating clinician (Slide 2). There are several factors that clinicians should consider in order to best distinguish these disorders, and ensure an accurate diagnosis—age of symptom onset, presenting symptoms, and family history of either disorder.

SLIDE 1
Comorbidity Rates of Major Depressive Disorder/Dysthmia and Adult ADHD[1]



ADHD=attention-deficit/hyperactivity disorder.

Age of Onset

Typically, ADHD presents first in children, whereas most mood disorders, specifically MDD, have their index case onset in adolescence. Although MDD and dysthymia is reported in childhood,[6,7] the peak incidence occurs during the adolescent years. Thus, the age of onset becomes one diagnostic factor that can assist in distinguishing these two conditions.

Presenting Symptoms

Presenting symptoms of ADHD and MDD seem to overlap but can be distinguished. While MDD is primarily a disturbance in mood, ADHD is a disturbance in cognition. As defined by the *Diagnostic and Statistical Manual of Mental Disorders*, Fourth Edition (*DSM-IV*)[8] the criteria for MDD diagnosis include sad mood and/or reduced motivation for 2 weeks accompanied by negative thoughts, apathy, hopelessness, and neurovegetative changes in sleep or appetite, among other symptoms.

In contrast, ADHD presentation is comprised of symptoms in the domains of inattention and hyperactivity/impulsivity.[8] Research in child populations has shown that the distribution of ADHD subtypes is: combined type (both inattentive and hyperactive/impulsive symptoms present) is ~65% of

SLIDE 2
Diagnostic Distinctions: MDD vs. Adult ADHD

MDD	Adult ADHD
Primarily a disturbance in mood	Primarily a disturbance in cognition
Sad mood/reduced motivation/negative thoughts/apathy/hopelessness/change in sleep and appetite	Inattention/distractibility/impulsivity/hyperactivity/making careless mistakes/forgetfulness/poor follow through/easily frustrated/interrupting behavior
Episodic	Chronic, pervasive, and impairing
First occurrence typically presents in teens	First symptoms typically presents in childhood
Mood disorders family history	Family history for ADHD

Both disorders may occur concurrently

MDD=major depressive disorder; vs.=versus; ADHD=attention-deficit/hyperactivity disorder.

Dr. Goodman is director of the Adult Attention Deficit Disorder Center of Maryland and Suburban Psychiatric Associates in Lutherville, and assistant professor in the Department of Psychiatry and Behavioral Sciences at Johns Hopkins School of Medicine in Maryland.

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all ADHD cases, the inattentive subtype represents ~30%, and the hyperactive/impulsive type is <5%.[9] However, these rates have not been well determined in the adult population. Overall, ADHD symptoms include inattention, distractibility, impulsivity, hyperactivity, forgetfulness, and poor follow-through as well as being easily frustrated, making frequent careless mistakes, and interrupting during conversation.

The time course of each disorder is also a distinguishing factor. Recurrent MDD tends to be cyclic and episodic while ADHD tends to be chronic, pervasive, and impairing over time. Although cognitive impairment may accompany an MDD episode, when the episode remits, in most cases, the cognitive symptoms remit as well. This result does not occur in ADHD. With concomitant MDD, cognition may worsen during the MDD episode, but after the remission of the depressive episode, the cognitive impairment persists in the patient with comorbid ADHD.

Family History

Often, there is a family psychiatric history of mood disorders in patients with MDD, typically in contrast to patients with ADHD. However, research by Biederman and colleagues[10] demonstrates that this simple relationship may not be clear. They examined 140 probands with ADHD, 120 normal controls and 822 first-degree relatives using blinded rater and structured interviews. Compared to relatives of controls, relatives of probands with ADHD had higher rates of ADHD, major depression, anxiety disorders and substance abuse. It is not clear if the disorders were comorbidities with ADHD.

Diagnostic Prioritization

Of adults with ADHD, 40% present with a concurrent active psychiatric condition that should be evaluated. Often a particularly challenging aspect of diagnosis is when a patient presents for a psychiatric or primary care evaluation with complaints of anxiety and depressed mood as an outgrowth of stressful consequences in their life, such as job loss, marital conflict, and/or disappointment in social relationships. In this circumstance, the clinician should question and evaluate for the presence of ADHD as symptoms of ADHD have often produced the negative consequences that have resulted in complaints of depressed mood and anxiety. ADHD should be evaluated in adults in every initial psychiatric evaluation because the prevalence rate of adults with ADHD is 4.4%, which is higher than the prevalence rate for schizophrenia (1%), bipolar disorder (2.5%), and generalized anxiety disorder (3%).[11,12]

The Texas Algorithm—which was developed for use in treatment recommendations and is an outgrowth of child and adolescent literature—states that clinicians should treat the most severe comorbid disorder first.[13] Thus, clinicians should determine the severity of the other comorbid disorders to choose further treatment options. If the child presents with severe MDD and ADHD, then the MDD should be treated first followed by initiation of ADHD treatment. However, if the child presents with dysthymia and ADHD, then the recommendation is to treat the ADHD and re-evaluate the dysthmia for subsequent treatment. However, in adult psychiatry, this treatment course may be problematic if a patient presents with a depressive episode and the clinician does not evaluate for bipolar disorder. If the clinician believes that the ADHD is so severe that it should be treated first, there exists the risk that the bipolar disorder will be exacerbated by the initiation of ADHD medication in an untreated bipolar patient (Slide 3).[14]

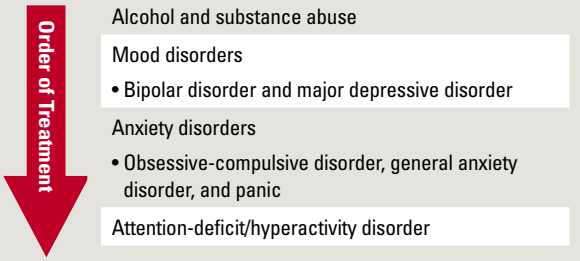
There will be further treatment modifications that will evolve as the adult research in comorbid psychiatric conditions with ADHD emerges. Unfortunately, given the paucity of research in the treatment of comorbid disorders with ADHD, it is currently a steep learning curve for clinicians.

Pharmacologic and Psychotherapy Treatment Options

Comprehensive treatment including pharmacologic and psychotherapeutic approaches will produce the most optimal response to treatment. Currently, there are five medications specifically recommended for ADHD treatment: d-methylphenidate extended release (XR), OROS methylphenidate, mixed amphetamine salts XR, lisdexamfetamine, and atomoxetine. All of these agents are long-acting, once-daily medications; there are no short-acting stimulant medications specifically US Food and Drug Administration-indicated to treat adults with ADHD. In contrast to short-acting stimulants, long-acting agents control symptoms throughout the day, and are less likely to provoke mood changes when their effects wear off. This eliminates confusion regarding patients' moods being an outgrowth of their underlying mood disorder versus an adverse event from the stimulant medication.

As polypharmacy is often the treatment for many patients with comorbid disorders, it is important to understand drug-drug interactions, both kinetic and dynamic. In regards to kinetics, FDA-approved ADHD medications do not have inhibitory effects on cytochrome P450 (CYP) enzymes and therefore will not alter the metabolic kinetics of other medications. (Slide 4).[14] As to dynamic interactions, there may potential

SLIDE 3
Diagnostic Prioritization for Pharmacotherapy[14]



Treatment order also considers severity of the concurrent disorders.

SLIDE 4
CYP Inhibitory Effects of ADHD Medications[14]

	CYP Isoenzymes				
Medication	***1A2***	***2C9***	***2C19***	***2D6***	***3A4***
Amphetamine	0	0	0	0	0
Methylphenidate	0	0	0	0	0
Atomoxetine	0	0	0	0*	0
Bupropion	?	?	?	+++	?
Desipramine	0	0	0	0	0

* In vivo.
CYP=cytochrome P450; ADHD=attention-deficit/hyperactivity disorder.

additive effects that increase the likelihood of adverse events (ie, lithium and stimulants increasing fine digital tremor).

Bupropion—which is not indicated for the treatment of ADHD, although there are positive adult controlled trials—does have a significant inhibitory effect on CYP 2D6, which should be considered when using substrates that are metabolized through CYP 2D6, (eg, atomoxetine).[15]

In the pharmacologic treatment of ADHD, it is important for clinicians to consider nonadherence to medication (Slide 5).[16] This is an issue not only for patients with ADHD, but also an issue for patients with MDD; the nonadherence rate at 4–6 months is ~50% for either disorder. Thus, nonadherence to medical treatment for these conditions leads to a likely nonadherence or partial treatment of other concomitant medical conditions. This is an area that needs further exploration in adult ADHD as it has impact on the long term treatment of medical illnesses, such as hypertension, heart disease, and diabetes.

In addition to pharmacologic treatments for both disorders, there are psychotherapeutic treatments available to clinicians. There are several therapeutic approaches that have been researched. Controlled trials have demonstrated significant benefit from the addition of cognitive behavioral therapy (CBT) to ADHD medication beyond the benefit of medication alone.[17,18] CBT has been demonstrated to be highly effective in MDD disorders. Unfortunately, there is no quality research on the use of CBT in concurrent MDD and ADHD.

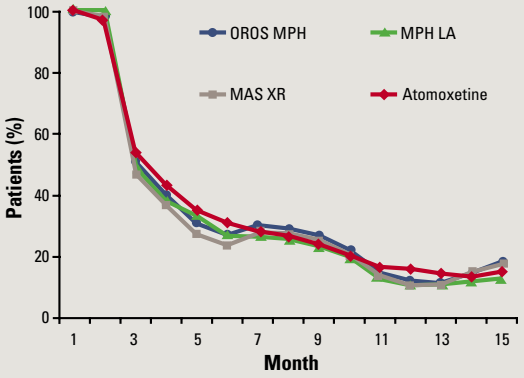
Conclusion

ADHD in adults occurs at a prevalence rate (4.4%) that is higher than many major psychiatric disorders in adults. In those adults for whom this is a persistent and impairing condition, it should be appreciated and treated as a life-long disorder. In addition, the rates of psychiatric comorbidities with adult ADHD are higher than many major psychiatric disorders. Diagnostic challenges exist in accurately determining ADHD in the presence of concurrent active psychiatric disorders. Often the overlap of symptoms makes the delineation of disorders very difficult. Once the psychiatric disorders have been enumerated in the patient, the clinician then needs to determine a diagnostic prioritization in order to formulate a pharmacologic algorithm. The object is to treat one disorder without destabilizing or worsening the other disorders. Although there are no formal guidelines for treating coexisting psychiatric disorders with ADHD in adults, the preliminary treatment approach suggests treating and stabilizing alcohol/substance abuse first, then severe MDD or bipolar disorder, then severe anxiety disorders, and lastly ADHD. There is research on treating concurrent substance abuse and ADHD which demonstrates that treating ADHD in the presence of untreated substance abuse results in small improvements in ADHD symptoms without much change in the substance abuse. This suggests that treatment of substance abuse needs to be at least concurrent with, if not preceding, treatment for ADHD.

There are no controlled trials showing the treatment of MDD, bipolar disorder, or the anxiety disorders in adults with ADHD. Therefore, clinicians cannot find guidance in the research for the treatment of ADHD and comorbidities. Treatment options are both pharmacologic and psychotherapeutic. Currently, there are five medications specifically FDA-approved for the treatment of ADHD in adults: lisdexamfetamine, OROS-methylphenidate, dexmethylphenidate XR, mixed amphetamine salts XR, and atomoxetine. All of these medications have long durations of action. Specific therapeutic approaches have demonstrated efficacy in controlled trials and should be offered to and individualized for the patient. A thoughtful evaluation process accurately delineating the presenting psychiatric disorders will facilitate the diagnostic prioritization necessary to formulate a treatment algorithm for an optimal outcome.

SLIDE 5

Adherence Rates of ADHD Medications[15]



ADHD=attention-deficit/hyperactivity disorder; OROS MPH=OROS methylphenidate; MPH LA=methylphenidate hydrochloride extended release; MAS XR=mixed amphetamine salts extended release.

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BIPOLAR DISORDER AND ADHD: *CLINICAL CONCERNS*

Roger McIntyre, MD, FRCPC

Introduction

During the past decade, a similar composite has emerged for both bipolar disorder and adult attention-deficit/hyperactive disorder (ADHD). First, both conditions have a relatively high prevalence, a low case detection, a protracted illness course, a high rate of comorbidity, multifactorial ideology, substantial heritable liability, and tremendous burden of illness in economic cost as well as interpersonal and vocational maladjustments. What has also been interesting along with these reports is that there has been emerging scientific studies implicating common brain regions and neural circuits subserving essential features of both conditions.[1-7]

There has also been an interest in characterizing and reporting the prevalence of ADHD in patients who do have well-characterized bipolar disorder. Although results from epidemiological studies are few in number, they are large in their impact. Results from the National Comorbidity Survey Replication indicate that ~20% of respondents who screened positive for bipolar disorder will also screen positive for ADHD.[4]

Clinical studies on bipolar disorder and ADHD in adults are also few in number, but large in their sample size. The largest systematic evaluation of ADHD adults in bipolar populations characterized in a clinical sample was reported by the Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-BD).[8] This study reported an overall lifetime prevalence of adult ADHD of 9.5%; by gender, the rate was reported as 14.7% for males and 5.8% for females.[8]

What is important for clinicians and researchers to remember is that debate and lack of consensus continues to exist in our field regarding the validity of diagnosing ADHD in adults who have bipolar disorder. One of the challenges to accurate diagnosis is the commonality of both conditions, with the lifetime rate of bipolar spectrum disorders currently reported at ~2% to 4%.[9] This is a rate not entirely dissimilar from the rate of adult ADHD. The issue of symptom overlap between both conditions is an area of diagnostic confusion for many practitioners. For example, some of the features of mania—such as crowded or racing thoughts, distractibility, increased activity or physical restlessness, and loss of "normal" social inhibitions—are features not only encountered in mania but may be encountered in some patients who have adult ADHD.

Phenomenology and Progression

However, there are some important differences between the phenomenology of adult ADHD and bipolar disorder. First, there exists a longitudinal difference between the two conditions. ADHD phenomenology tends to be chronic in its expression, while, classically, bipolar disorder tends to be episodic, in many cases becoming chronic, but more classically episodic. Secondly, adult patients with ADHD do not typically report increased productivity or increased psychomotor activity resulting in productive changes. Classically, patients with bipolar disorder will report increased activity, which would correspond with an increase in energy. Thirdly, patients with ADHD do not typically report a decreased need for sleep or inflated self-esteem, which are very common features in bipolar disorder. Also, what may be a particularly distinguishing feature between bipolar disorder and adult ADHD is the presence of psychoses, such as delusions, hallucinations, or thought disorder. These are not features that are commensurate with a diagnosis of adult ADHD.[10]

Past research has shown that depressive symptoms and episodes dominate the course of bipolar disorder. Not only do depressive symptoms and episodes dominate the course of bipolar disorder but they portend much of the psychosocial, interpersonal, and workforce maladjustment that is documented in patients with bipolar disorder. It is now believed that much of the cost of illness in bipolar disorder is driven by depressive symptoms, and in the United States, bipolar disorder is considered the most costly psychiatric disorder.[11]

Notwithstanding these important phenomenological differences, clinicians continue to struggle with understanding where the interface or the diagnostic boundary is between ADHD and bipolar disorder. However, the overarching question remains—what is the relevance of diagnosing ADHD in a bipolar population? The relevance is underscored by results from the STEP-BD initiative.[8] That study reported that patients with bipolar disorder who also met criteria for adult ADHD reported an earlier age of onset of the bipolar disorder. It is also understood that earlier age of bipolar disorder onset is a more virulent bipolar disorder when compared to more typical age onset, in early adulthood or later in life. The STEP-BD group also found shorter well intervals—the time from the onset of one affective episode to the time of onset of the second affective episode—which indicated a greater cyclicity and propensity for affective relapse.

Moreover, the STEP-BD group reported that patients with bipolar disorder and ADHD had a greater propensity to depression, more depressive episodes, and higher rates of psychiatric comorbidity, typically in the form of comorbid anxiety disorders, substance use disorders, as well as a history of aggression and violence. Aggression and/or violence, in many unfortunate situations, can result in confrontation with law enforcement and others. Taken together, the co-occurrence of adult ADHD with bipolar disorder adds to the overall illness burden. Comorbidity carries with it diagnostic and treatment implications as well as a worsened prognosis for the patient.

Dr. McIntyre is associate professor of psychiatry and pharmacology at the University of Toronto, and head of the Mood Disorders Psychopharmacology Unit at the University Health Network in Toronto, Canada.

Disclosures: Dr. McIntyre is on the advisory boards of AstraZeneca, Biovail, Bristol-Myers Squibb, Eli Lilly, GlaxoSmithKline, Janssen-Ortho, Lundbeck, Organon, Pfizer, Schering-Plough, Shire, and Solvay/Wyeth; is on the speaker's bureaus of AstraZeneca, Biovail, Eli Lilly, Janssen-Ortho, Lundbeck, and Wyeth; receives grant/research support from Eli Lilly, Janssen-Ortho, the National Alliance for Research on Schizophrenia and Depression, Shire, and the Stanley Medical Research Institute; and receives honoraria from AstraZeneca, Bristol-Myers Squibb, and Solvay/Wyeth. Dr. McIntyre discusses unapproved/investigational uses of psychostimulants for the treatment of attention-deficit/hyperactivity disorder.

ADHD and Bipolar Disorder Treatment

Regarding the treatment of bipolar disorder in ADHD, first it is important to begin with guiding principles for treating bipolar disorder pharmacologically. The current recommendations for treating bipolar disorder as presented in several evidence-based guidelines and algorithms, which are either evidence or consensus based, is the usage of US Food and Drug Administration-approved agents for treating bipolar mania or the depressive phase of bipolar disorder.[12,13]

The past 10 years has seen more agents approved for various phases of bipolar disorder than there have in the past 10 decades combined. It is important that treatment selection and sequencing take into consideration the phase of illness. The foundation of treating bipolar disorder is pharmacotherapy. Along with pharmacotherapy and, as part of a larger chronic disease management model, a clinician should consider integrating psychosocial treatment approaches and educational approaches in a longitudinal care program.

The same principles of treating bipolar disorder would not be dissimilar for treating ADHD in terms of the fact that it is a chronic disease; chronic disease management principles are warranted. The pharmacologic foundation of treating ADHD in adults includes the use of psychostimulants, which are the first line agents. Other agents include atomoxetine as agents of alternative choice.

The question clinicians often struggle with is the hazard posed by utilizing stimulants or agents that may possess stimulant-like properties in a patient who has bipolar disorder. Generally, there is a concern that has been supported by evidence that stimulants may in fact carry a hazard for mobilizing an affective episode (a hypomanic, mixed, or manic episode) in the short term or may destabilize bipolar disorder with long-term exposure.[12,13]

The avoidance of psychostimulants in bipolar disorder substantiates ideology over analysis of the data, meaning that there are no large, randomized, double-blind, placebo-controlled trials that have evaluated the safety or efficacy of any stimulant or stimulant-like agent for ADHD in bipolar disorder. The concern around the use of stimulants relates in part to open-label data, chart reviews, consensus, and in some cases, clinical experience.[14] Nevertheless, there is no "Level 1" evidence—randomized, double blind, placebo controlled studies—in adult populations.

Notwithstanding the absense of evidence available in adult populations, there is one small randomized, double-blind, placebo-controlled trial in a pediatric sample of patients with bipolar disorder in ADHD.[15] This study enrolled patients (N=40) and stabilized their bipolar symptomatology with divalproex. When bipolar symptomatology was stabilized, subjects were then assigned to either mixed amphetamine salts, combination, or placebo. All subjects were evaluated with usual measures of bipolar disorder in ADHD. What we learned from this pediatric sample is that the adjunctive use of a psychostimulant in this population not only improved the ADHD features when compared to placebo, according to change in Young Mania Rating Scale baseline scores, but seemed to exert a salutary effect on the bipolar symptoms as well. This one study suggested that the use of stimulants is effective in treating ADHD phenotype in bipolar children and adolescents with the guiding principle being that the mood should be stabilized first.

Although a non-stimulant, there have been cases of atomoxetine inducing mania in adults with bipolar disorder and caution is urged for use in child populations due to increased mania/hypomania induction and mood dysregulation for those with bipolar disorder and ADHD.[16]

Clinicians are often familiar with being in situations where they must make treatment decisions in the absence of an unequivocal evidentiary base, and the ADHD bipolar adult is no exception. The guiding principle in treating this condition is to choose an agent and select an algorithmic treatment for bipolar disorder concordant with FDA-approved and evidence-based treatment guidelines. If and/or when the patient continues to manifest features of ADHD, despite the fact mood stabilization has been optimized and affective symptoms have been well-controlled, then the adjunctive use of a psychostimulant could be used. However, there is no psychostimulant that is approved, proven to be efficacious, or established as safe for ADHD in adults with bipolar disorder comorbid with ADHD. All patients with bipolar disorder, regardless of ADHD comorbidity, should have their symptoms tracked with symptom measurement tools, such as a mood diary, to evaluate symptom severity, determine the efficacy of the intervention, and to provide an objective chronicling of symptoms over time.

The question also arises as to whether or not treatment with psychostimulants should be in the short-term or long-term in a patient with bipolar disorder. The guiding principle is that progress should be evaluated on a case-by-case basis, and the determination of whether or not a patient should be considered for continuation of long-term therapy would be based on short-term treatment outcomes, in terms of efficacy and tolerability, buttressed by clinical ratings.

Conclusion

There are now several lines of evidence, from epidemiological and clinical studies, that indicate that ADHD adult phenotype is a common occurrence in bipolar disorder. What is key is that ADHD in the adult population comprises an important therapeutic target insofar as ADHD in the adult population carries implications for course of illness, symptom presentation, and prognosis. Empirical trials that are adequate in their design and sufficiently powered to address the questions that clinicians ask on a daily basis are eagerly awaited. In the interim, the safe and judicious use of stimulants may be warranted in some carefully-selected patients in an effort to reduce ADHD symptoms and improve their overall functional outcome.

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SUBSTANCE USE DISORDERS AND ADHD

Oscar Bukstein, MD, MPH

Introduction

In examining the challenges in treating comorbid attention-deficit/hyperactivity disorder (ADHD) and substance use disorder (SUD), there are a number of issues regarding misinformation and misconception that exist for clinicians. Like other ADHD comorbidities, there is a lack of screening, particularly among adult clinical populations who have the psychiatric comorbidity or, for patients with SUDs, there is the issue of prioritization, which condition to treat first, and determining the place of medication management—particularly stimulant medication—paramount in treatment planning.

ADHD and SUD Prevalence

Regarding comparative prevalence, ADHD is more prevalent in community populations of patients with SUDs. Data from a study of ~2,000 adults admitted to substance use treatment programs in multi-site studies found that ~33% of adults also met criteria for ADHD.[1] This result confirms data from a number of clinical populations of patients with SUDs, where the non-comorbid prevalence of ADHD is increased. In a general population study covering 10 countries, including the United States and parts of Europe and the Middle East, for adults with an SUD, >11% endorsed meeting ADHD screening criteria.[2] As this result is not as extensive as in a clinical population, it still represents about a doubling of the prevalence found in the general population.

Interestingly, the relationship between ADHD and the development of SUD has received much attention in the literature over the past several decades. Most of the past literature suggested that the increased risk of SUD development in adolescence and into early adulthood was not due to the presence of ADHD alone, but rather due to the frequent comorbidity with conduct disorder, and that conduct disorder was the active risk factor.[3]

Similarly, more recent study results show some variability. For example, in a 25-year-old longitudinal study of a birth cohort in New Zealand, researchers found that conduct problems in childhood and adolescence were generally related to later substance use, abuse, and dependence, even after controlling for attention problems and confounders.[4] In addition, the authors found that attention problems were largely unrelated to later substance abuse, use, and dependence even after controlling for conduct problems and confounders.[4]

However, in a large prospective study of twins, researchers examined both dimensional and categorical measures of both ADHD and conduct disorder.[5] For both boys and girls, hyperactivity-impulsivity symptoms predicted initiation of all types of substance use, nicotine dependence, and cannabis use and dependence, even when controlling for conduct disorder at two separate time points. In contrast, relationships between inattention and substance outcomes disappeared when controlling for hyperactivity or impulsivity symptoms and conduct disorders, with the exception of nicotine dependence. A categorical diagnosis of ADHD significantly predicted tobacco and illicit drug use only and not abuse dependence of any kind.

Clinical Concerns in SUD Diagnosis

There are additional clinical concerns regarding SUD diagnosis, particularly regarding assessment, of which clinicians should be aware. Many of the same concerns that involve ADHD diagnosis in adults and screening apply to this type of comorbidity. However, it is more important that clinicians proceed with obtaining rating scales and using other informants, particularly to establish the developmental pattern of ADHD symptoms (Slide 1). Establishing age of onset of ADHD has been another concern for diagnosing ADHD. Although age of onset prior to age 7 is required by DSM-IV, those adults who meet all ADHD criteria except age at onset or those who meet subthreshold number of symptoms also have elevated rates of substance use and impairment.[6]

Many patients with any psychiatric comorbidity may present with the appearance of inattention or other cognitive deficits that are actually temporary and related to the abnormal state produced by that psychiatric comorbidity, such as SUD or mood disorder, for example. Thus, it is very important to use other informants and possibly review a paper record to establish that, these symptoms are indeed persisting and that these were preceding symptoms and not just produced by the psychiatric comorbidity (Slide 2).

Treatment Considerations

There have been ~15 well-controlled, randomized, or open studies that have a relatively large subject number on the treatment of ADHD and SUD. In studies that involve both stimulants and non-stimulants, there are several conclusions that become apparent to researchers.[3]

SLIDE 1
SUD in ADHD: Clinical Considerations

Is he or she a current drug abuser or past substance user?
- Established period of abstinence
- Ongoing substance abuse treatment

Is there a history of stimulant or amphetamine abuse?
- Reasons for past use: to get work done or to "get high"

SUD=substance use disorder; ADHD=attention-deficit/hyperactivity disorder.

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First, more studies are needed and current studies are inconclusive. Specifically, studies with more subjects and that incorporate alternative methodologies, such as inclusion of adjunct psychosocial interventions and alternative outcomes, are necessary. Second, studies in adults with ADHD-SUD comorbidity show that medications do appear to improve ADHD in adults with SUDs. Despite this apparent benefit, relatively robust findings that are found in open studies are only partially found when controlling for those studies: that is, much of the improvement noted is lost after controlling for variables.

Third, medications alone for ADHD do not appear to affect SUD. Although, they are valuable in treating the comorbidity of ADHD, medication does not appear to affect the substance use or the impairment resulting from the SUD, according to these studies.

Among the questions that occur from treatment literature are: will improvements in ADHD have positive effects on treatment and recovery from SUD? Prospective follow-up literature suggests that patients with comorbidities do not have outcomes better than patients without comorbidity.[3] This finding certainly extends to ADHD-substance use comorbidity. However, studies are needed that examine the treatment process, including psychosocial treatments, and examine the ability of patients who may receive ADHD medication to benefit from psychosocial treatment for SUDs when compared with those who do not receive ADHD treatment.

Treatment Recommendations

There are a number of emerging treatments that are available to clinicians. Typically, the use of long-acting stimulants allow for the treatment of some patients with histories of active substance use problems, with at least less risk of prompting dependence. This is due primarily to the issue of the less rapid action of long-acting stimulants. These medications are released into the brain at a slower rate and their peaks are delayed. Based on what is known about substance dependence, this would probably retard the development or exacerbation of dependence. This includes long-acting stimulant agents, such as methylphenidate, including OROS methylphenidate, dexmethylphenidate extended release, or amphetamines, such as mixed amphetamine salts or lisdexamfetamine.

There are non-stimulant agents that can be used, as well, and this includes the US Food and Drug Administration-approved atomoxetine. Many clinicians believe that these are the first-line drugs for substance abusing patients or those in SUD treatment, as opposed to being more tertiary drugs in many non-substance abusing samples. There are a number of other non FDA-approved or non-indicated non-stimulant medications, such as bupropion and modafinil. Modafinil recently has been shown to produce signs of dependence based on some imaging studies, but its risk relative to stimulants has yet to be determined.[6]

In addition, there are a number of agents in development, such as long-acting guanfacine, long-acting clonidine, or nicotinic receptor modulator, which may also be valuable in substance-dependent populations. As suggested by literature, psychosocial adjuncts are necessary and that ADHD treatment alone is not sufficient in patients with this comorbidity and that their SUDs should also receive clinicians' attention.[7]

SLIDE 2
SUD in ADHD: Clinical Recommendations

Stimulant use in substance-abusing patients is complex.

- Is the patient reliable?
- Are there family members or close nonsubstance-abusing friends involved in the treatment plan?
- Has patient/family been adequately informed of potential risks involved in using stimulants?

Have other options been tried?

- Atomoxetine, bupropion, desipramine, or modafinil

SUD=substance use disorder; ADHD=attention-deficit/hyperactivity disorder.

Treatment Safety

Along with understanding the safety concerns in treating ADHD patients with comorbid SUD, clinicians should also try to not view SUD as a unitary phenomenon; there are different levels of risk and a clinician must examine a number of issues before deciding whether to use medications or what medications to use. One area of risk would involve the patient's history. Is there a history of stimulant abuse or dependence, cocaine abuse or dependence, or related behavior that may make stimulants more risky in this population? Does the patient have a history or active alcohol dependence, cannabis abuse, or past unrelated behavior where a stimulant would pose less of a risk? Does the patient have a history of selling or diverting illicit drugs or prescription medication?

This creation of a risk hierarchy would allow clinicians to base interventions at a certain level. For example, lower risk patients with ADHD and substance abuse behavior may receive brief office interventions on substance abuse as well as certain skills, resources, and warnings about diversion, in addition to monitoring. That monitoring would increase as the risk for the patient became higher. Family involvement will generally help with mediating such risk. Progressing to higher risk patients with ADHD and SUD, monitoring should increase. The inclusion of urine drug screens to monitor other drug use becomes important. These patients often will not only need a higher level of care for SUD treatment, but there may be a further delay in initiating ADHD treatment. Typically, ADHD is considered a less emergent issue than SUD or a severe mood disorder. Lastly, in higher risk patients, the use of non-stimulants should be exhausted before consideration of stimulant medications.

It would be beneficial to establish a period of abstinence in any patient with SUD. However, as the search for empirical evidence that stimulants or other medications may actually help the treatment process, it is important to consider that patients may be starting some of these treatment options before completing active treatment or the acute phase of active treatment.

Misuse and Diversion

Safety concerns regarding misuse and diversion remain important for clinicians who treat this type of comorbidity, and it requires much oversight on the part of the clinician (Slide 3). Other drugs that may be potentially used by the patient and their interactions must be considered. Risk of any cardiovascular effects of concomitant drug use is also a concern. There are some additional red flags for diversion or misuse: emergency calls, continued evidence of substance

SLIDE 3
Safety Concerns Regarding Misuse and Diversion of Stimulants

- Clinician oversight
- Overdose potential
- Use with other stimulants
- Interaction with other non-stimulant drugs
- Users unaware of contraindications and precautions
- Cardiovascular risk due to lack of screening

SLIDE 4
Red Flags for Diversion or Misuse

- Emergencies
- Continued substance abuse evidence
- Demands for immediate-release compounds
- Repeated discordant pill count
- Lost prescriptions
- Continuously escalating doses
- Symptoms of psychosis (bipolar)
- Infrequent user

use, patient demands for immediate-release compounds as opposed to non-stimulant agents or long-acting stimulant agents, repeated discordant pill counts, lost prescriptions, continuously escalating doses, and somatic symptoms as well as symptoms of psychosis or unstable affect (Slide 4).

In order to handle potential red flags, there are a number of precautions that clinicians should take. Clinicians should limit and manage pills given to these patients. Urine toxicology screens should be obtained on a regular basis. Clinicians should also require frequent patient visits. If stimulants are used, long-acting agents should be the selected options, and it should be emphasized that these medications are for regular use. Lastly, in order to prevent misuse and diversion (particularly for the college-age population), clinicians should discuss safe storage with the patient and that patients not advertise their medications, whether to other family members, friends, and/or roommates to avoid medication being stolen and used without a prescription (Slide 5).

SLIDE 5
Precautions When Using Medications With Abuse Potential in Substance Abusers With ADHD

- Limit and keep track of pills
- Obtain urine toxicology screens regularly
- Frequent patient visits
- Use of long-acting preparations
- Emphasis to patient to take medications regularly on an as needed basis
- Discussion with patient regarding safe storage and not advertising medications

ADHD=attention-deficit/hyperactivity disorder.

Conclusion

ADHD is commonly found in populations comorbid with SUDs. Although the effect of ADHD on treatment outcomes requires further research, the presence of ADHD presents a salient target for treatment, particularly with medication. Clinicians who proceed with pharmacologic treatment of ADHD need to be knowledgeable about assessment, medication choices, and procedures to reduce the risk of abuse and or diversion of therapeutic agents.

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QUESTION-AND-ANSWER SESSION

Q: Because most psychiatric comorbid conditions commonly found with attention-deficit/hyperactivity disorder (ADHD) tend to be relatively acute and severe, can there be a circumstance when ADHD treatment would be more aggressive, or when a clinician may treat ADHD first rather than second?

Dr. McIntyre: In the area of bipolar disorder, if the patient is presenting to my office with a predominantly manic presentation with typical manic symptoms or a syndromal mixed state, I would not use a psychostimulant in that state. The more typical patient that clinicians encounter in the real world is a patient who presents with major depressive disorder (MDD) and various admixtures of hypomanic features, which historically has been referred to as depressive mixed states. Also, there has been the appellation "agitated depression." This is a bit more challenging. I discussed the principle of assuring that bipolar disorder is treated first and ADHD treated second, which is admittedly in some cases an arbitrary distinction. Nevertheless, there have been many situations I have encountered when patients have bipolar depression and have minimal features of the typical symptoms of hypomania, yet they have very prominent distractibility and very prominent problems with focusing themselves as well as cognitive problems. In that case, I have often found myself treating what I believed to be symptoms that would comport with ADHD as well as a major depressive episode in bipolar disorder. Granted, in that case, I am using a stimulant primarily to target some ADHD symptoms, and some may ask if there is an additional benefit in treating the depressive episode with a stimulant, which is an entirely different question. Thus, the principle of treating bipolar disorder first is very much the principle. The fine print would be that there are many cases of treating a depressed bipolar patient who is not progressing through mixed hypomania or mixed mania, where I may use a stimulant with an aim to target some of the ADHD features in this patient who is still not stable from bipolar disorder.

Dr. Goodman: I would address this question based on an issue of severity, of which bipolar disorder becomes the exception to this axiom. If I have a patient who has a clear MDD episode with ADHD, I treat the MDD first because the cognitive impairments from MDD may cause the ADHD to appear worse when, in fact, the cognitive symptoms, in part, are an outgrowth of the MDD episode. In contrast, if a patient presents with dysthymia and ADHD, I am more likely to treat the ADHD first because dysthymia may be secondary to ADHD and may not be a primary mood disorder. The same treatment plan is true for anxiety disorders: if a patient has an active, acute panic disorder, I am more likely to treat that disorder before I treat ADHD. However, if the patient has mild generalized anxiety disorder, I would be more likely to treat ADHD symptoms first. It is important to make these diagnostic distinctions because the medications used for a number of these psychiatric conditions are so effective that we often lose sight of making diagnostic categorizations and just use selective serotonin reuptake inhibitors or other antidepressants for both anxiety and MDD. Sixty percent of MDD patients, though, present with anxious features. Data from the Sequenced Treatment Alternatives to Relieve Depression (STAR*D) study shows that those patients with anxious MDD are significantly less likely to respond to antidepressants.[1] These patients not only take longer to respond to antidepressants, but they are also more likely to report adverse events with their use. In looking at considerations for treating ADHD, anxious depressed patients may present who are more sensitive to stimulant or ADHD medication in regards to adverse events. That is how I would make those distinctions.

Q: For colleagues in substance use disorder (SUD) clinics who make use of naltrexone, naloxone, and disulfiram, what are some insights concerning the treatment of adults with ADHD who are on these medications and considering the ADHD medications available to them?

Dr. Bukstein: There is essentially no data on concomitant use of ADHD medications with these medications. ADHD medications, generally stimulants, do not affect the pharmacokinetics of very many agents. My own experience with buprenorphine indicates that these can be used particularly with stimulants without significant problems. I would imagine with norepinephrine reuptake inhibitors, some patient populations may have more difficulty. One of the reasons for treating comorbid ADHD is to reduce the many risk factors prompting patients to relapse in SUD treatment. Although many treatment professionals would want to keep treatment simple, many should look at polypharmacy in the addiction area. Those drugs that are most likely to produce the greatest effect on impairment and improvement in functioning should be added. Nevertheless, we have had incidental use of these agents without problems. There have been few reactions in terms of use with agents like naltrexone and disulfiram, although specific reactions have been found with stimulants or atomoxetine.

Q: For those clinicians who say the substance abuse is self-medication for ADHD, will treating the ADHD cause the SUD to improve?

Dr. Bukstein: That did not happen in any study. Among the ~15 studies that have reasonable sample sizes or reasonable control, including randomization, medicating the patient for ADHD did not improve the SUD, although researchers found variable rates of improvement of ADHD. Thus, in facilitating treatment and facilitating recovery, there is nothing actively that ADHD treatment does for SUD. Therefore, clinicians have to rely on psychosocial treatment for SUD as a concomitant treatment, along with medication management. It is pretty much required. What we do not know is if concurrent medication treatment for ADHD increases the long term success of SUD treatment.

Q: This question is often asked by clinicians in practice: an adult patient who has an MDD episode, and there is also reason to suspect that they may have ADHD. What does evidence show about psychostimulant use or other related agents as augmentation in patients who have MDD and are not responding to conventional therapy?

Dr. Goodman: Literature on stimulants in depressive disorders exists since the 1970s and 1980s when there was a limited number of agents, and patients were simply not responding or were intolerant to medication.[2] Research has shown that if stimulants are given to patients with MDD, improvement occurred. Even when stimulants are given to the general population, people report an improvement in energy,

QUESTION-AND-ANSWER SESSION

mood, concentration, and motivation, and this improvement is simply the psychological experience of increasing dopamine and norepinephrine in the brain. For patients with refractory MDD, stimulants are a useful adjunct in combination with an antidepressant. There are studies showing that the use of stimulants in medically hospitalized patients reduced MDD, increased adherence and compliance to medical treatment, reduced length of stays, and reduced the overall cost of medical care.[3] Stimulants fell out of favor because the mood benefit diminished with long term use. Thus, there was a belief that a patient may show diminishing improvement over time, then the clinician must either increase the dose or find a new alternative antidepressant treatment. For those patients with adult ADHD and MDD, I treat the MDD first and track the rate of response. If the patients has a partial response to the antidepressant with continuing ADHD, the question becomes do you continue to pursue an antidepressant regime aggressively until remission, or would you accept a reasonably partial response to the antidepressant and then add a stimulant with the hope that you would be able to treat two conditions simultaneously? Would I advocate using stimulants alone to treat MDD and ADHD? Currently, we do not have any literature to support that treatment course. Although it is sensible, that would not be my first treatment choice.

Dr. Bukstein: It is interesting in the world of children and adolescents where clinicians are more likely to, particularly in the case of mild comorbidities, treat the ADHD first and track any secondary effects on mood.

Q: Stimulants have been shown to be beneficial for ADHD, but clinicians are often concerned about using them in bipolar patients. There is virtually no evidence on their safety except by expert consensus. There are now colleagues in the bipolar arena who are taking an opponent position on this use, which is generating division within psychiatry. What do you foresee the future portends in trying to create a mutual understanding and satisfactory approach to concomitant bipolar disorder and ADHD in adults?

Dr. McIntyre: I do believe that the categorical proscription and ananthematizing of psychostimulants in the short- or long-term treatment of bipolar disorder is an example of ideology over analysis. There is an ethos in the field that psychostimulants should not be prescribed in bipolar populations due to their hazardous effects. There is only one adequately designed study that is powered sufficiently to address this question.[4] It is a pediatric study, and the results of that study cohere with the experience of many clinicians: a psychostimulant added to an anticonvulsant that possesses some degree of mood stabilization properties, such as divalproex, improves symptoms that are thought to be part of an ADHD diagnosis without destabilizing bipolar disorder.[4] However, one study is not enough to result in a large-scale shift in opinion, but it is an important piece of evidence that militates against some of the opinion. I believe that the lack of consensus that currently exists in the field of bipolar disorder regarding the use of conventional antidepressants has been instructive, and I think it provides a context of how to think about the use of psychostimulants. Antidepressant usage in bipolar disorder, in jurisdictions where they are available, are used frequently in bipolar disorder, yet researchers debate as to whether or not they should be used. The most rigorous of evidence—randomized, double-blind, placebo-controlled trials—does not provide a compelling story of efficacy. It does indicate some degree of efficacy in the short-term with antidepressants, and also does not provide compelling evidence of destabilization in the short-term. Therefore, some of these issues are influenced by a risk: benefit analysis: is ADHD symptomatology in a bipolar patient a therapeutic target that I should prioritize? I think that is what drives usage. In fact, based on the evidence, such as data from the Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-BD),[5] which found that ADHD does pose a serious hazard in bipolar disorder, and their experience, clinicians should find a way to safely treat ADHD. The clarion call is for a large randomized controlled trial in the adult population. The therapeutic index of these agents needs to be better characterized in adults; but what is clear is that it is virulently comorbid in bipolar disorder.

Dr. Goodman: Bipolar experts may say that the STEP-BD study showed that antidepressants are no more effective than placebo for bipolar depression.[5] Also, it took the field 25 years to realize that antidepressants caused cyclicity, and that maybe in 20 years from now—after stimulants are so broadly prescribed—there will be an understanding that they, too, do for bipolar disorder what antidepressants have been shown to cause.

Dr. McIntyre: Clinical research has not yet unequivocally established that antidepressants result in cycle acceleration in bipolar disorder. It is quite possibly the case that there are subpopulations that are vulnerable to this unwanted event, the inclusion of heterogeneous samples may obfuscate this finding. In keeping with this view, it is reasonable to hypothesize that there may be a subset of patients susceptible to destabilization with psychostimulants but it is unlikely the case that this is a vulnerability equally shared amongst most bipolar populations. Also, the notion that antidepressants are universally inefficacious and are harmful is again another example of ideology over analysis. Clearly, unimodal antidepressants have an underwhelming therapeutic index in bipolar disorder, which, I believe, has been an observation found by many clinicians. The primary reason antidepressants are used in bipolar disorder is because the condition is so virulent, and therefore the decisions around benefits and risks are affected by that course. The same is true for the stimulants. Thus, careful scrutiny of antidepressant data in bipolar disorder provides a fertile ground for important debate on principles of management in bipolar disorder.

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DIFFERENTIAL DIAGNOSIS OF ADULT ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: TREATMENT OPTIONS AND COMORBIDITY CONSIDERATIONS

CME QUESTIONS

1. **What is the approximate prevalence rate of adult attention-deficit/hyperactivity disorder (ADHD) in patients with acute major depressive disorder (MDD)?**

   A. 1 in 3
   B. 1 in 5
   C. 1 in 10
   D. 1 in 20

2. **What factor will not aid in distinguishing MDD and ADHD?**

   A. Clinical interview for presenting mood and cognitive symptoms
   B. Family history for depressive disorders or academic struggles
   C. Age symptoms first occurred
   D. Previous diagnosis of the disorder
   E. Cognitive improvement in response to stimulant treatment

3. **In the treatment with medications for ADHD in patients with comorbid substance use disorder (SUD), which of the following is true:**

   A. ADHD symptoms are improved
   B. SUD behaviors are improved
   C. Both ADHD and SUD are improved
   D. Side effects were too great to justify treatment

4. **The Texas Treatment Algorithm has been established for the treatment of ADHD and comorbid psychiatric disorder in children, adolescents and adults.**

   A. True
   B. False

5. **Psychostimulants increase risk of medication switch based on randomized controlled trials with placebo.**

   A. True
   B. False

6. **Regarding the prevalence of ADHD in populations of persons with SUD, which of the following is true:**

   A. Comorbidity is present in <10% of patients
   B. Comorbidity is present in >70% of patients
   C. Comorbidity is present in ~33% of adult patients
   D. Comorbidity is more common in community populations than in clinical populations

7. **Which of the following options are not recommended precautions when using medications with abuse potential in substance abusers with ADHD:**

   A. Limit and keep track of pills
   B. Obtain urine toxicology screens regularly
   C. Frequent patient visits
   D. Use of short-acting preparations

8. **ADHD is common in bipolar disorder but does not affect course of bipolar disorder illness.**

   A. True
   B. False

REGISTRATION

JULY 2009 CME POSTTEST

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ANSWER FORM

Expert Panel Supplement – Differential Diagnosis of Adult Attention-Deficit/Hyperactivity Disorder: *Treatment Options and Comorbidity Considerations*

TERMINATION DATE: July 31, 2011

To receive credit, you should score 70% or better (participants will receive certification for their records in approximately 4–6 weeks). Early submission of this posttest is encouraged. Please submit this test by July 1, 2011, to be eligible for credit. If you have any questions about this, or any of our other CME materials, please e-mail CME@mblcommunications.com

Please circle your answers

1. A B C D 2. A B C D E 3. A B C D 4. A B 5. A B 6. A B C D 7. A B C D 8. A B

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