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PRACTICAL MANAGEMENT STRATEGIES FOR ACUTE MANIA AND MIXED EPISODES OF BIPOLAR DISORDER: *MEDICAL COMORBIDITY AND RECOVERY IN INDIVIDUALS WITH BIPOLAR DISORDER*

FACULTY

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CME .25

ABSTRACT

Bipolar disorder is a lifelong condition, which is diagnosed according to corroborative features such as family history, chronobiological sensitivities, treatment outcomes, longitudinal course, and patterns of recurrence. Each illness state is also classified as involving pure mania, hypomania, a mixed episode, a depressed phase, or euthymia. Mixed states are thought to comprise an important subgroup of syndromically ill individuals with bipolar disorder. Several dimensions of psychopathology, including thought-language problems, behavioral disturbances, mood symptoms, and chronobiological changes demand careful evaluation when considering the presentation of a patient with bipolar disorder. Once a comprehensive diagnostic assessment for acute or mixed mania has been completed, it is important to look at an evidence-based data set to guide treatment selection for mood stabilization. Pharmacotherapy is essential to its long-term management of bipolar disorder. Combination therapy, including at least one mood stabilizer, may be necessary to treat acute depression and mania and to further prevent both depressive and manic recurrences. The goal is to minimize frequency, duration, and severity of depressive and manic symptoms with a treatment regimen that is positioned to maximize treatment adherence and minimize side effects. Prevention of mania and maintenance treatment in bipolar disorder is largely routed in the decision to use monotherapy or combination therapy in the treatment regimen. Treatment must also include consideration of comorbidities such as anxiety, substance abuse, cardiovascular disease, and metabolic syndrome, which are pervasive in the bipolar disorder population.

In this Expert Review PsychCast™, Martha Sajatovic, MD, focuses on medical comorbidity and recovery in individuals with bipolar disorder, with particular focus on the medical burden of mania, aging and bipolar disorder, and treatment approaches that promote functional recovery.



This activity is jointly sponsored by the Mount Sinai School of Medicine and MBL Communications, Inc.



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Activity Review Information

The activity content has been peer-reviewed and approved by

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Review Date: November 30, 2009

Faculty Affiliation

Martha Sajatovic, MD, is professor of psychiatry at Case Western Reserve University School of Medicine in Cleveland, Ohio

Faculty Disclosure Policy Statement

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Faculty Affiliations and Disclosures

Dr. Sajatovic has received research support from AstraZeneca and GlaxoSmithKline.

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

Dr. Haznedar is assistant professor of psychiatry, at Mount Sinai School of Medicine. Dr. Haznedar reports no financial, academic, or other interest in any organization that may pose a conflict of interest.

Learning Objectives

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

- Propose rational treatment strategies for patients with bipolar disorder and medical comorbidity that address patient safety and long-term health outcomes

Statement of Need and Purpose

Bipolar disorder, a chronic episodic disease that is present in ~5.7 million Americans, is a complicated condition. No single medication or therapy is effective in treating bipolar disorder, and recent evidence suggests that subtypes of the disorder have been underrepresented due to the bipolar spectrum of expression. While the prototypic clinical picture concerns the "classic" bipolar disorder, mixed episodes with incomplete recovery and significant psychosocial impairment are more frequent and comprise up to 40% of acute bipolar hospital admissions. The clinical presentation of these mixed episodes is variable and eludes contemporary classification systems. Patients with mixed episodes tend to have a more severe course of illness compared to those with classic euphoric manias. They have less frequent remissions, higher rates of recurrence, more frequent substance abuse, poorer response to some medications, more extensive comorbidities, and increased potential for suicidality. Despite the available medications, treating mixed states remains a challenge and tends to require more complex treatment. Rational dosing is a problem as many trials do not address dosing questions. In addition, when and how to combine medications has not been studied nor is the issue of which medications should be discontinued during maintenance stages. Treatment ultimately depends on the patient's individual need and his or her psychiatric and medical comorbidities. The presence of a comorbid substance use disorder is associated with significantly lower rates of treatment adherence, higher anxiety disorder comorbidity, more suicide attempts, and poorer outcome, especially in terms of functioning and quality of life. Psychoeducation in combination with efficacious drug therapy may improve outcomes of patients with acute and mixed episodes of bipolar disorder.

Target Audience

This activity is designed to meet the educational needs of primary care physicians and psychiatrists.

Accreditation Statement

This activity has been planned and implemented in accordance with the Essential Areas and policies of the Accreditation Council for Continuing Medical Education (ACCME) through the joint sponsorship of the Mount Sinai School of Medicine and MBL Communications, Inc. The Mount Sinai School of Medicine is accredited by the ACCME to provide continuing medical education for physicians.



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The Mount Sinai School of Medicine designates this educational activity for a maximum of .25 *AMA PRA Category 1 Credits*™. Physicians should only claim credit commensurate with the extent of their participation in the activity.

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Listen to this Expert Panel PsychCast™, reflect on the information presented, and complete the CME posttest and evaluation on pages 6 and 7. To obtain credit, you should score 70% or better. Early submission of this posttest is encouraged. Please submit this posttest by April 30, 2012 to be eligible for credit.

Selected content from this supplement will be available via ePocrates MobileCME in 2010.

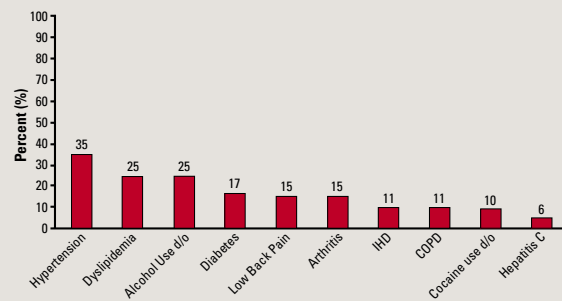


MEDICAL COMORBIDITY AND RECOVERY IN INDIVIDUALS WITH BIPOLAR DISORDER

By Martha Sajatovic, MD

SLIDE 1

Common Medical Conditions in Patients with Bipolar Disorder¹



IHD=ischemic heart disease; COPD=chronic obstructive pulmonary disease.

SLIDE 2

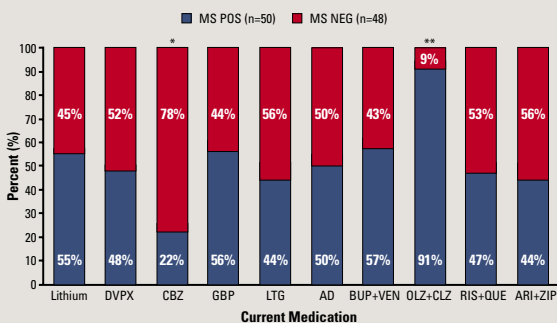
Cardiovascular Disease Risk Factors¹⁻³

Estimated Prevalence and Relative Risk (RR)

Modifiable Risk Factors	Schizophrenia	Bipolar Disorder
Obesity	45–55%, 1.5–2 x RR	21–49%, 1–2 x RR
Smoking	50–80%, 2–3 x RR	54–68%, 2–3 x RR
Diabetes	10–15%, 2 x RR	8–17%, 2 x RR
Hypertension	19–58%, 2–3 x RR	35–39%, 2 x RR
Dyslipidemia	25%, ≤5 x RR	23%, ≤5 x RR

SLIDE 4

Metabolic Syndrome in a Bipolar Cohort (n=98)⁴



MS=metabolic syndrome; DVPX=divalproex; CBZ=carbamazepine; GBP=gabapentin; LTG=lamotrigine; AD=antidepressant; BUP=bupropion; VEN=venlafaxine; OLZ=olanzapine; RIS=risperidone; QUE=quetiapine.

SLIDE 3

Metabolic Syndrome and Bipolar Disorder⁴⁻¹⁶

Study	Definition of MS	MS Prevalence
Cardenas et al (2008) ⁴	NCEP ATP III	49%
Chang et al (2009) ⁵	IDF 2005	33.9%
Correll et al (2008) ⁶	NCEP ATP III	43.2%
Elmslie et al (2009) ⁷	NCEP ATP III	50%
Fagiolini et al (2008) ⁸	NCEP ATP III*	40%
Fiedorowicz et al (2008) ⁹	NCEP ATP III	>50%
Garcia-Portilla et al (2008) ¹⁰	NCEP ATP III†	22.4%
John et al (2009) ¹¹	IDF	67%
Salvi et al (2008) ¹²	NCEP ATP III IDF	25.3% 30%
Sicras et al (2008) ¹³	NCEP ATP III	24.7%
van Winkel et al (2008) ¹⁴	NCEP ATP III NCEP ATP III* IDF	16.7% 18.3% 30%
Vuksan-Cusa et al (2009) ¹⁵	NCEP ATP III	27.5%
Yumru et al (2007) ¹⁶	NCEP ATP III	32%

NCEP ATP III: ≥3 of the following—waist circumference: >102 cm men, >88 cm women; triglycerides: ≥150 mg/dL; HDL-C: <40 mg/dL men, <50 mg/dL women; blood pressure: ≥130/85 mmHg; fasting glucose: ≥110 mg/dL. Modified ATP same as ATP III except—fasting glucose: ≥100 mg/dL, or treatment for hypertension, hyperlipidemia, and hyperglycemia. IDF—two criteria and waist criterion met: waist: ≥94 cm men, ≥80 cm women; triglycerides: ≥150 mg/dL; HDL-C: <40 mg/dL men, <50 mg/dL women; blood pressure: ≥130/85 mm Hg; fasting glucose: ≥100 mg/dL. IDF 2005 same as IDF except—waist: ≥90 cm men.

* Modified

† Modified (NHANES 1999–2000)

MS=metabolic syndrome; NCEP=National Cholesterol Education Program; ATP=adult treatment panel; IDF=International Diabetes Federation; HDL-C=high density lipoprotein-cholesterol; NHANES=National Health and Nutrition Examination Survey.

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SLIDE 5

*Measures to Minimize and Manage Medical Comorbidity in Patients with Bipolar Disorder*¹⁷

Treatment factors:

- Appropriate baseline and follow-up assessments of metabolic parameters; body mass index
- Selection of pharmacotherapy that minimizes patient vulnerability to adverse effects

System factors: coordination with primary and specialty care as needed

Behavioral modifications: exercise, nutrition, substance abuse monitoring/treatment

SLIDE 6

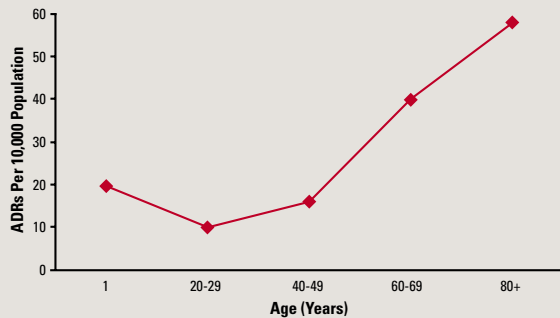
Late-Life Bipolar Disorder Is Common in Clinical Populations^{18,19}

In contrast to rather low rates in the community:

- 6% of geriatric outpatient visits
- 8% to 10% of geriatric inpatient admissions
- 3% of nursing home residents
- 17% of geriatric patients presenting to psychiatric emergency department
- Individuals with bipolar disorder continue to experience illness burden across the life-span; illness does not go away or “burn out” in late life

SLIDE 7

*Adverse Drug Reactions (ADRs) As a Function of Increasing Age*²⁰



SLIDE 8

*Factors Affecting Plasma Drug Concentration Achieved*²¹

Age

Gender

Genetics (hepatic enzyme polymorphism)

Administration (time of day, food effect)

Body habitus (size, percentage of body fat, nutritional status)

Physiological derangement (comorbid disease, impaired organ function)

Pharmacokinetic drug interactions (concomitant medications, toxins)

SLIDE 9

*Acute Pharmacotherapy of Late-Life Mania Study (GERI-BD)*²²

9-week randomized, double-blind, concentration-controlled parallel group trial in bipolar manic, mixed, and hypomanic patients >60 years of age

Aims

- To compare the tolerability and side effects of lithium and valproate
- To compare the efficacy of lithium and valproate for psychopathology, function, and quality of life over 9 weeks
- Preliminary description at baseline (N=100)
 - Mean age=68.9 years (SD 7.13, range 60–84 years)
 - 50% Female, 86% white, mean of 13.4 years of education (SD±3.14).
 - Mean baseline Young Mania Rating Scale 26.38 (SD±6.73)

SLIDE 10

Summary: Managing the Older Patient with Bipolar Disorder or the Patient With Bipolarity and Medical Comorbidity

Characterize target symptoms: mania, depression/subsyndromal symptoms

Perform medical evaluation to identify/manage comorbid medical disorders

Review medication regimen

- Assess adverse effects (toxicity/withdrawal)

Employ behavioral interventions

Pharmacotherapy needs a parsimonious, step-wise approach that utilizes available evidence from medically complex/elderly populations

- Baseline
- Ongoing

Conduct a multidisciplinary coordination

- Adequate monitoring and follow-up

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PRACTICAL MANAGEMENT STRATEGIES FOR ACUTE MANIA AND MIXED EPISODES OF BIPOLAR DISORDER— MEDICAL COMORBIDITY AND RECOVERY IN INDIVIDUALS WITH BIPOLAR DISORDER

CME QUESTIONS

- 1. Metabolic syndrome occurs in which of the following proportion of patients with bipolar disorder?**
 - A. 3% to 5%
 - B. 5% to 10%
 - C. 20% to 60%
 - D. 80%
- 2. All of the following statements are true of later-life bipolar disorder, except:**
 - A. It is relatively uncommon in the general geriatric population
 - B. It occurs in 17% of geriatric patients presenting to the psychiatric emergency department
 - C. It tends to “burn out” as an individual ages
 - D. Medical comorbidity is more common than in younger populations
- 3. Adverse drug reactions remain relatively low in early adulthood and then begin to increase sharply after the 8th decade of life.**
 - A. True
 - B. False
- 4. Which is not a common medical condition in patients with bipolar disorder?**
 - A. Diabetes
 - B. Hypertension
 - C. Jaundice
 - D. Alcohol use disorders

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APRIL 2010 CME POSTTEST



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ANSWER FORM

CME PSYCHCAST™ – Practical Management Strategies for Acute and Mixed Episodes of Bipolar Disorder—
Medical Comorbidity and Recovery in Individuals with Bipolar Disorder

TERMINATION DATE: April 30, 2012

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 April 1, 2012, to be eligible for credit. If you have any questions about this, or any of our other CME materials, please e-mail CME@mbllcommunications.com

Please circle your answers

1. A B C D 2. A B C D 3. A B 4. A B C D

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