

Diagnosing and Managing Depressive Episodes in the DSM-5 Era

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Talk 1: Unipolar or Bipolar Depression?

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Mood disorders can be considered to exist on a disease continuum. Depressive disorders comprises a spectrum of disease that can be difficult to distinguish and therefore challenging to treat. Recent changes to the DSM criteria need to be taken into account by both clinicians and researchers. Notably, in the updated DSM-5, a mixed episode as defined in DSM-IV-TR (“juxtaposed full manic and depressive episodes”) was removed.¹ In its place, subthreshold non-overlapping symptoms were added using a “with mixed features” specifier, which can be applied to either major depressive disorder or bipolar I or II disorder. The new classification may present challenges to clinicians and researchers.² Depressive symptomatology, whether related to bipolar or unipolar disease, could substantially benefit from improvements in identification. Better identifiers of specific depressive disorders, such as phenomenological characteristics,³⁻⁶ improved screening tools⁷ or biomarkers,^{8,9} may facilitate better diagnosis. This talk includes a discussion of the spectrum of mood disorders; an overview of epidemiology, phenomenology, biomarkers, and the DSM-5; and discussion of the “with mixed features” specifier in approaching the diagnosis of depression.

1. American Psychiatric Association . *Diagnostic and Statistical Manual of Mental Disorders*. Arlington, VA: American Psychiatric Association; 2013.

2. Vieta E, Valenti M. Mixed states in DSM-5: implications for clinical care, education, and research. *J Affect Disord*. 2013;148(1):28-36.

3. Berk M, Berk L, Moss K, Dodd S, Malhi GS. Diagnosing bipolar disorder: how can we do it better? *Med J Aust*. 2006;184(9):459-462.

4. Galvao F, Sportiche S, Lambert J, et al. Clinical differences between unipolar and bipolar depression: interest of BDRS (Bipolar Depression Rating Scale). *Compr Psychiatry*. 2013;54(6):605-610.

5. Motovsky B, Pecenak J. Psychopathological characteristics of bipolar and unipolar depression - potential indicators of bipolarity. *Psychiatr Danub*. 2013;25(1):34-39.

6. Perlis RH, Brown E, Baker RW, Nierenberg AA. Clinical features of bipolar depression versus major depressive disorder in large multicenter trials. *Am J Psychiatry*. 2006;163(2):225-231.

7. Zimmerman M, Chelminski I, Young D, Dalrymple K, Martinez JH. A clinically useful self-report measure of the DSM-5 mixed features specifier of major depressive disorder. *J Affect Disord*. 2014;168:357-362.

8. Powell TR, McGuffin P, D'Souza UM, et al. Putative transcriptomic biomarkers in the inflammatory cytokine pathway differentiate major depressive disorder patients from control subjects and bipolar disorder patients. *PLoS One*. 2014;9(3):e91076.
9. Redlich R, Almeida JJ, Grotegerd D, et al. Brain morphometric biomarkers distinguishing unipolar and bipolar depression. A voxel-based morphometry-pattern classification approach. *JAMA Psychiatry*. 2014;71(11):1222-1230.

Talk 2: Treating Depression in the Presence of Manic and Hypomanic Features: What's New?

Mark A. Frye

Although unipolar depression has relatively clear treatment recommendations, treatment resistance makes depression difficult to treat in many patients.^{1,2} Misdiagnosis of bipolar depression as unipolar depression may contribute to treatment resistance.³ Depression is predominant in bipolar disorder but compared with acute mania has less systematic research guiding treatment development.⁴ Currently only quetiapine, the olanzapine-fluoxetine combination, and lurasidone are FDA-approved for depression in bipolar disorder,⁵ by comparison with the glut of agents for bipolar mania, highlighting a need in this area. Antidepressants are the most commonly prescribed drugs for depression in bipolar disorder,⁶ despite the evidence being much stronger for their efficacy in unipolar than bipolar depression. The conclusion of the recent International Society for Bipolar Disorders Task Force on Antidepressant Use in Bipolar Disorders is that it is not possible to make recommendations regarding antidepressants and that non-antidepressant treatments, including lithium, lamotrigine, olanzapine, quetiapine, and lurasidone, should be considered as monotherapy before using antidepressants in bipolar depression.⁷ In addition, the new "with mixed specifier" makes differentiation of unipolar depression from bipolar depression increasingly complex, leading some to propose that the unipolar depression with mixed features should in fact be classified as bipolar disorder.⁸ Recent data indicate that lurasidone is effective in treating unipolar depression with mixed features.^{9,10} This talk highlights new pharmacologic approaches to the management of depression in the face of manic and hypomanic features.

1. Rush AJ, Trivedi MH, Wisniewski SR, et al. Acute and longer-term outcomes in depressed outpatients requiring one or several treatment steps: a STAR*D report. *Am J Psychiatry*. 2006;163(11):1905-1917.
2. Trivedi MH, Rush AJ, Wisniewski SR, et al. Factors associated with health-related quality of life among outpatients with major depressive disorder: a STAR*D report. *J Clin Psychiatry*. 2006;67(2):185-195.
3. Dervic K, Garcia-Amador M, Sudol K, et al. Bipolar I and II versus unipolar depression: Clinical differences and impulsivity/aggression traits. *Eur Psychiatry*. 2015;30(1):106-113.

4. Frye MA, Prieto ML, Bobo WV, et al. Current landscape, unmet needs, and future directions for treatment of bipolar depression. *J Affect Disord.* 2014;169(S1):S17-S23.
5. Fountoulakis KN, Gazouli M, Kelsoe J, Akiskal H. The pharmacodynamic properties of lurasidone and their role in its antidepressant efficacy in bipolar disorder. *Eur Neuropsychopharmacol.* 2015;25(3):335-342.
6. Baldessarini RJ, Leahy L, Arcona S, Gause D, Zhang W, Hennen J. Patterns of psychotropic drug prescription for U.S. patients with diagnoses of bipolar disorders. *Psychiatr Serv.* 2007;58(1):85-91.
7. Pacchiarotti I, Bond DJ, Baldessarini RJ, et al. The International Society for Bipolar Disorders (ISBD) task force report on antidepressant use in bipolar disorders. *Am J Psychiatry.* 2013;170(11):1249-1262.
8. Liu X, Jiang K. Should major depressive disorder with mixed features be classified as a bipolar disorder? *Shanghai Arch Psychiatry.* 2014;26(5):294-296.
9. McIntyre RS, Cucchiaro J, Pikalov A, Kroger H, Loebel A. Lurasidone in the treatment of bipolar depression with mixed (subsyndromal hypomanic) features: post hoc analysis of a randomized placebo-controlled trial. *J Clin Psychiatry.* 2015;76(4):398-405.
10. Pikalov A. 15th International Congress on Schizophrenia Research (ICOSR). Abstract 2114720. Presented March 31, 2015.

Talk 3: Complex Case Presentations: Depression with Subsyndromal Mania and Hypomania, and Syndromal Mania and Hypomania with Subsyndromal Depression

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Faculty members will discuss diagnosis and management of a series of complex patients in the light of the previous presentations