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SAN FRANCISCO, April 25 -- Dysphoric mania and other mixed mania states of bipolar disorder will become easier to diagnose with better definitions, a researcher said here.

"We don't have a very clean way to capture all the mixed states," said Trisha Suppes, M.D., Ph.D., of the University of Texas Southwestern Medical Center at Dallas. She presented working definitions and an algorithm for treatment here at the U.S. Psychiatric and Mental Health Congress regional extension.

The current Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) includes a definition for mixed episode, which is one that meets the diagnostic criteria for both a manic episode as well as a major depressive episode nearly every day for at least a full week.

However, it does not include a definition for dysphoric mania or hypomania, Dr. Suppes said. One contemporary definition of "unhappy mania," or "energized depression" as she describes it to patients, is an episode that meets criteria both for manic or hypomanic episode and simultaneous presence of at least three depressive symptoms.

She said an expansion of the mixed states definition is on the docket for the next edition of the DSM, to which she is a contributor.

"I think this is one of the main reasons why we miss folks with bipolar disease on evaluation at presentation," she said.

The full mixed episode category affects about a third of patients with bipolar disorder, predominantly women. A study in the Journal of the American Medical Association in 1994 reported that 38% of patients hospitalized with acute mania had mixed or dysphoric mania.

Dr. Suppes said it is even more common for patients further along in the course of the disorder -- 10 to 15 years -- who continue to cycle.

Mixed episodes are a volatile mix of lowered action threshold and "incredible" dysphoria that brings more suicidal ideation and attempts and more comorbid substance abuse disorders than euphoric, or "pure," mania, she added.

Dr. Suppes and colleagues conducted a study following 908 bipolar patients in the Stanley Foundation Bipolar Network for two years and found that their affective state was mixed hypomania at 4.2% of all office visits, depressed at 34% of visits, and hypomanic at 3.1%.

She said she hopes this empiric data will get into the DSM update as well.

"The diagnosis is being missed and folks aren't getting the treatment they need," she said.

Treatment for mixed states overall appears to be about as effective with the atypical antipsychotic medications as for manic episodes, she said. Adding an antidepressant to a mood stabilizing medication does not make depression better in these patients and actually makes the mania worse, she added.
"The therapeutic challenges are many," Dr. Suppes said, but she presented an evidence-based algorithm that she helped develop. It was published in the Journal of Clinical Psychiatry in 2005.

For bipolar disorder type I patients who are in a mixed manic or hypomanic state, she recommended valproate, aripiprazole (Abilify), risperidone (Risperdal) or ziprasidone (Geodon) as initial treatment with olanzapine (Zyprexa) and clozapine (Clozaril) as alternate choices. Nonresponders should be put on an alternate monotherapy.

Stage two, for patients who get only partial response is to try a two-drug combination of lithium and valproate or an atypical antipsychotic. They should not be put on two atypical antipsychotics or given aripiprazole or clozapine.

For those who get no response, stage three is a two-drug combination of lithium, valproate, an atypical antipsychotic (not two and not clozapine), carbamazepine, oxcarbazepine (Trileptal), or a typical antipsychotic.

Stage four includes electroconvulsive therapy or adding clozapine or the combination of lithium, an atypical antipsychotic, and valproate, carbamazepine, or oxcarbazepine.

Controversies about mixed states include gradations of subsyndromal mania or hypomania in depression, she said. "Mixed depression is not operationalized in the DSM but is clinically recognized," she said.

Dr. Suppes defined mixed depression as syndromal depression with intra-episode hypomanic or manic symptoms not meeting DSM criteria.

Dr. Suppes reported receiving grants and research support from Abbott, AstraZeneca, Bristol-Myers Squibb, GlaxoSmithKline, JDS Pharmaceutical, Janssen, National Institutes of Mental Health, Novartis Pharmaceuticals, The Stanley Medical Research Institute and Wyeth/Solvay. She also reported having served as a consultant or on the advisory board for Abbott, AstraZeneca, Bristol-Myers Squibb, Eli Lilly and Company, Janssen, JDS Pharmaceuticals, GlaxoSmithKline, Novartis Pharmaceuticals, Ortho-McNeil Pharmaceutical, Pfizer, Shire Pharmaceutical, UCB Pharma, and Wyeth/Solvay.

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