

in hormonal effects on brain and behavior, and for revealing mechanisms that confer sex-related differential risk for neuropsychiatric disorders. Moreover, the potential importance of such gene–hormone interactions suggests a general strategy for further exploration that may inform individualized treatments.

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Sex differences in the incidence of antidepressant-induced mania (AIM) in bipolar disorders

Aislinn Williams¹ and Melvin G. McInnis² 

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Bipolar disorder has similar prevalence between the sexes, but evidence suggests that men and women experience the disorder differently. Disorder onset, comorbidities, and treatment diverge significantly between men and women. For example, depressive episodes seem to predominate bipolar illness episodes in women, whereas in men, mania is more frequent [1]. There are also sex differences in management of medication side effects and comorbidities [2], and women with bipolar disorder report poorer sleep quality, which predicts more intense mood symptoms [3].

An oft-cited but poorly understood phenomenon in bipolar disorder is antidepressant-induced mania (AIM) or antidepressant emergent manic symptoms (AEMS). AIM describes the observation that hypomanic and manic symptoms can emerge when bipolar disorder patients use antidepressants, particularly when they are not taking a concurrent mood stabilizing medication. However, most bipolar disorder patients do not develop AIM when exposed to antidepressants, and the current data suggest that the risk factors for AIM in men and women may differ [4]. Clinicians routinely screen for AIM when treating bipolar depression with antidepressants, but little is known about which demographic and clinical variables increase risk for AIM, and even less is known about gender-specific risk factors.

In our retrospective study of 416 patients with bipolar disorders, we found that women were more likely to receive antidepressants than men [5]. This is in agreement with data from Karanti et al. [6] who showed that women with bipolar disorder were more likely to be prescribed antidepressants than men, which was independent of illness severity or other clinical factors. Strikingly,

in our sample, female sex was the only variable that emerged from regression modeling as a statistically significant risk factor for AIM. In another recent study, Scott et al. [4] identified a number of factors that convey differential risk for AIM between men and women. They reported that male AIM patients were more likely to have an alcohol or substance use disorder, a history of suicide attempt(s), and a greater number of depressive episodes per year. Female AIM patients were more likely to have a history of thyroid disorder, family history of bipolar disorder type I, or a depressive episode at the onset of bipolar illness.

These early findings of differences between men and women with bipolar disorder, and how this may affect the incidence of AIM, are compelling and merit further study. Tools for identifying patients at highest risk would be very helpful, particularly since the incidence of AIM is low (generally estimated to be ~10–20% of bipolar disorder patients who take antidepressants) but the dangers of mania are significant. It is unclear whether the observed treatment and outcome discrepancies between men and women with bipolar disorder are due primarily to physiological differences between sexes (e.g., hormonal pathways, sex-specific neuronal circuitry), or as described in Karanti et al [6], have less basis in physiology and more to do with disparities in how physicians treat women and men (Fig. 1).

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¹Assistant Professor of Psychiatry, University of Iowa, Iowa City, IA 52242, USA and ²Department of Psychiatry, University of Michigan, 4250 Plymouth Road, Ann Arbor, MI 48109, USA

Correspondence: Melvin G. McInnis (mmcinis@umich.edu)

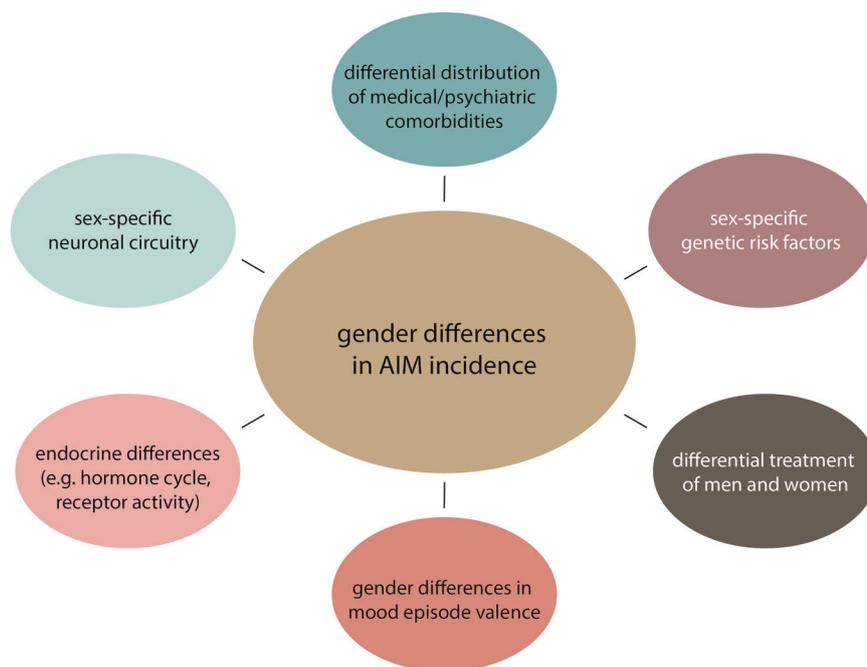


Fig. 1 Potential factors that contribute to gender differences in antidepressant-induced mania

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Guidance cues: linking drug use in adolescence with psychiatric disorders

Lauren M. Reynolds^{1,2} and Cecilia Flores²

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Adolescent onset of drug use is associated with an enduring elevation in the risk of progressing from recreational use to addiction. Unfortunately, adolescent experimentation with

drugs of abuse remains common, with more than half of initiates under the age of 18 years old. This peak age for drug initiation coincides with a critical developmental period for

¹Integrated Program in Neuroscience, McGill University, Montréal, QC, Canada and ²Department of Psychiatry and Department of Neurology and Neurosurgery, McGill University, Douglas Mental Health University Institute, Montréal, QC, Canada
Correspondence: Cecilia Flores (cecilia.flores@mcgill.ca)

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