

New Uses for Old Drugs and New Circuits for Old Disorders

By Eric Hollander, MD

This month, we explore the expanding use of anticonvulsants in neuropsychiatry, specific brain circuits associated with postpartum depression (PPD), and some unusual medical presentations of endocrine dysfunction in patients.

Khalid I. Afzal, MD, David F. Briones, MD, and Cecilia DeVargas, MD, describe a 15-year-old Hispanic female who, on risperidone, developed rapid weight gain (12 pounds in 16 days), polydipsia, and polyphagia. She also complained of nipple discharge and abdominal pain, and her prolactin level increased to three times normal. On switching to another antipsychotic, her prolactin level dropped to normal, she lost the weight, and her abdominal pain, galactorrhea, polydipsia, and polyphagia subsided.

Fayez El-Gabalawi, MD, and Robert Arnold Johnson, MD, describe a 17-year-old girl with hypersexuality due to virilization, a consequence of polycystic ovarian syndrome. The authors also review the literature on hypersexuality in children and adults. They define hypersexuality as sexual behaviors or fantasies that have abruptly increased in frequency by comparison with a previous baseline, or are of sufficient excessiveness to disrupt expected or usual social, academic, or occupational functioning, or constitute a source of distress. In their patient, the authors present a differential diagnosis for hypersexuality, and, while virilization is not a common cause, it should not be overlooked.

Anticonvulsants are increasingly being used by psychiatrists and neurologists in a broad range of disorders other than bipolar disorder,

epilepsy, and migraine. Jennifer M. Rosenberg, MD, MPH, and Carl Salzman, MD, review the literature on the use of anticonvulsants and lithium in substance use disorders, anxiety disorders, and schizophrenia. Given the difficulties of prescribing benzodiazepines for alcohol and benzodiazepine withdrawal, they believe anticonvulsants are an alternative. Promising therapeutic effects have been demonstrated in many of the anxiety disorders, with the greatest positive results in posttraumatic stress disorder. Although anticonvulsant and lithium augmentation for schizophrenia is common, the evidence has been inconclusive.

I would also note that our group at the Mount Sinai School of Medicine and others have studied the use of anticonvulsants in cluster B personality disorders, such as borderline personality disorder, as well as developmental disorders, such as autism, with considerable success. Some of these agents, such as valproate, have unique properties in addition to their effects on γ -aminobutyric acid, such as enhancing brain-derived neurotrophic factor and neuroplasticity; as an histone deacetylation inhibitor with potent epigenetic effects; as an anti-kindling agent; and by enhancing enzymes that convert glutamate to γ -aminobutyric acid.

With the prevalence of HIV on the rise and almost 20% of HIV patients suffering from neurologic comorbidity due to HIV itself, antiretroviral medications, or other HIV-related comorbidities, it is imperative that clinicians and physicians be able to address any such complications in those

in their care. In their case report, Daniel Costello, MD, MRCPI, describe the cognitive, behavioral, and neuropsychiatric disturbances in detail in order to illustrate the range of manifestations of disordered mental states associated with encephalopathy in three HIV-infected individuals. The authors clearly emphasize the possibility of cognitive-behavioral dysfunction being the dominant presentation of HIV infection.

Up to 760,000 women suffer annually from PPD, yet <50% of these cases are recognized. Michael E. Silverman, PhD, and colleagues probe the neuropathophysiology of postpartum depression and identify fronto-limbic-striatal dysfunction. Identifying this specific brain circuitry may have an impact on diagnostic systems, such as the *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition*, increase our understanding of the spectrum of affective disorders, shed light on possible mechanisms responsible for PPD, and provide a foundation for the development of more targeted biologically based diagnostic and therapeutic strategies for PPD. An unresolved but important question is whether identifying specific brain circuitry dysfunction in

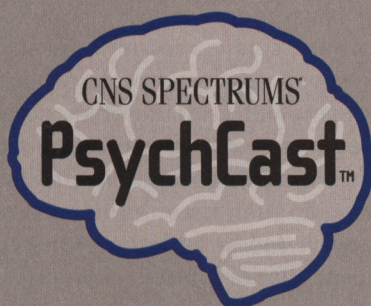
a unique patient (as opposed to mean values in a diagnostic category) may have a direct impact on diagnosis and treatment selection.

In this month's issue, we also continue our new section, "In Session," a series of interviews by Norman Sussman, MD, with leaders in our field on various topics of interest. Here, we feature an interview with Stephen R. Marder, MD, professor of psychiatry at University of California, Los Angeles, who describes how he views the differences between clinical trials and clinical experience with the newer atypicals, and interprets some of the take-home messages of the Clinical Antipsychotic Trials of Intervention Effectiveness Study.

Happy Thanksgiving. **CNS**

ERRATUM

The title of the "Consensus Statement." *CNS Spectr.* 2007;12(Suppl 3):59-63 in the February 2007, supplement, "From Obsessive-Compulsive Spectrum to Obsessive-Compulsive Disorders: The Cape Town Consensus Statement," was incorrectly printed. The title should be "Consensus Statement on Obsessive-Compulsive Disorder."



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