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## **Focus on Addiction: Bupropion for Cocaine Relapse and Monitoring Controlled Substances Prescribed to Dually Diagnosed Patients**

The new Focus on Addiction section will strive to cover a range of topics in addiction medicine. While future issues will also include investigations of behavioral and neurobiological mechanisms, this month's inaugural section features a clinical trial and an epidemiologic survey that address two key issues in addiction medicine today: pharmacotherapy of psychostimulant addiction and the alarming rise of prescription drug misuse.

The clinical trial, by Winhusen and colleagues, is informed by the extensive preclinical research pointing to the limbic dopamine D<sub>3</sub> receptors as a promising therapeutic target for cocaine use disorder.<sup>1</sup> While compounds with a specific D<sub>3</sub> receptor binding profile are still being developed for clinical use,<sup>2</sup> bupropion, which is a safe and well-tolerated FDA-approved anxiolytic agent binding both serotonin and dopamine D<sub>3</sub> receptors, provides a unique opportunity to explore a potential heuristic value of targeting the D<sub>3</sub> receptor. To that end, Winhusen and colleagues conducted a National Institute on Drug Abuse-sponsored trial involving double-blind, placebo-controlled administration of 15 to 60 mg/d of bupropion to individuals with cocaine use disorder. Sixty-two participants (37% female) were followed for 12 weeks after inpatient detoxification. Careful attention was given to the monitoring of abstinence (primary outcome) and to treatment adherence. Self-report data on recent drug use were automatically matched to the urine toxicology findings, while adherence to the study medicine was ascertained with the medication event monitoring system and biochemical assays. In this trial, bupropion did not seem to separate from placebo, with women showing worse outcomes than men. This result, extending a previously reported lack of efficacy of bupropion in non-detoxified current users,<sup>3</sup> is thought provoking. First, it resonates with the data on gender differences in cocaine addiction, which link vulnerability to relapse to the greater severity of depressive symptomatology, along with family and social problems, in cocaine-dependent women versus men.<sup>4</sup> Second, it highlights the fact that the bench-to-bedside translation is often not straightforward.<sup>5</sup> Although the negative outcomes of this trial lower the expectations for bupropion, the trial provides additional impetus for the clinical testing of more specific dopamine D<sub>3</sub> receptor agents as well as of higher-than-anxiolytic doses of bupropion.<sup>2</sup>

The second article, a CME activity, reports on the ongoing pandemic<sup>6,7</sup> of prescription medications abuse. Hackman et al used records from Indiana's statewide prescription drug monitoring program (PDMP) to extract and analyze patterns in the prescription of opioid and benzodiazepine drugs. In 37 states,<sup>8</sup> it is mandatory for pharmacists to record filled controlled substance prescriptions in such systems, and the databases are accessible to licensed prescribers and law enforcement officers. The authors examined electronic records of 201 individuals treated in "dual diagnosis" clinics over a 12-month period. The sample was 51% female, and two-thirds of surveyed individuals were uninsured. Over 80% were dually diagnosed with a substance use disorder, including opioid dependence, and psychotic, mood, or anxiety disorders. On average, patients received 213 opioid pills by 4 different prescriptions from 2.6 providers; nearly 20% were prescribed both an opioid and a benzodiazepine. More opioid prescriptions and a greater number of prescribers directly correlated with opioid dependence and personality disorder diagnoses, respectively. While the study findings per se provide no

information about the appropriateness of the prescriptions, they illustrate 2 important clinical problems: (1) patients who are at risk for the development of drug use disorders are more likely to be prescribed pharmacologic agents with addictive potential, and (2) comorbidity of addictive and other psychiatric disorders is quite prevalent, and more research is needed on epidemiology and treatment of such conditions. The study also offers helpful leads on how to reduce “doctor shopping” and encourages greater utilization of PDMPs for estimating the true amount of controlled substances dispensed to an individual.

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