**Dextromethorphan: Another “Ecstasy”?**

The letter by Cranston and Yoast in the April issue of the Archives, which discusses the abuse potential of dextromethorphan (DMX), is timely because it is a readily available substance that was recently distributed in Texas at “rave” parties as the newest ecstasy. Rave parties are all-night dances that were originally popularized by European adolescents at which loud “techno” music is played and at which euphoriant drugs called ecstasy are usually available. Ecstasy refers to methamphetamine drugs, but can also be composed of gamma hydroxybutyrate and ma huang/ephedra. Because DMX is legal and is widely available on the Internet in quantities large enough to be abused, we’d like to address a few points that need clarification. First, the authors stated that “dextromethorphan is a nonopioid drug.” Actually, DMX is an opioid; it is the D-isomer of levorphanol, a semisynthetic morphine derivative. Dextromethorphan undergoes metabolic O-demethylation to its active metabolite dextrorphan, which has similar activities to phencyclidine. Second, in addition to the triad that they describe, which includes ataxia, nystagmus, and altered mental status, seizures also may occur at 20 to 30 mg/kg. Euphoria and hallucinations occur in doses from 300 to 1800 mg/kg (20 or more times the dose in a teaspoonful). Dextromethorphan has an onset of action within 15 to 30 minutes, and peaks in 2.5 hours, with duration of action between 3 to 6 hours. Lastly, DMX can interact with monoamine oxidase inhibitors, causing severe hyperthermia, and may cause serotonin syndrome. Dextromethorphan inhibits the metabolism of norepinephrine and serotonin and blocks the reuptake of serotonin. Physicians need to be aware of the abuse potential of DMX, as well as the availability of drug information on the Internet. Adolescents can download instructions on making illicit substances, as well as purchase the ingredients necessary to create these dangerous products. Finally, physicians need to remember that DMX is found as a component of a large number of nonprescription cough and cold remedies, usually in combination with decongestants, antihistamines, and acetaminophen. These other compounds have toxic properties that are independent of dextromethorphan and may require specific treatment.

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disorders, 1 psychotic disorder, 1 somatoform disorder, and 2 sleeping disorders. In 3 cases, substance-related disorders were also diagnosed. Of the 21 patients with mood disorders diagnosed by the GP, 12 could theoretically be treated with selective serotonin reuptake inhibitors.

In line with Klinkman et al, we found a substantial number of false-positive GP diagnoses of mood disorders. Moreover, in nearly half of these patients, another serious mental disorder was found, and, in a few patients, no mental disorder could be established. We agree with the editorial by Block7 that GPs should not only make precise diagnoses of mood disorders but also should look to other significant mental disorders, especially when misidentification can have therapeutic implications.

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In reply

We appreciate the interest in the clinical importance of accuracy of mood disorder classification shown by van Rijswijk and colleagues. They contend that the importance of DSM-IV–level precision in primary care diagnosis may be overstated, as several disorders may be treated with the same general approach, such as treating both major depressive disorder (MDD) and general anxiety disorder with selective serotonin reuptake inhibitors. They cite their own findings of Nijmegen general practitioner identification of mood disorders, which showed that a substantial proportion of patients with false-positive diagnoses of MDD had other serious mood disorders (eg, generalized anxiety disorder, dysthymia) that could be treated in the same way as MDD.

In our study, we were also able to establish the presence of other psychiatric disorders in our subjects, as all completed the Structured Clinical Interview for DSM-III-R at entry. Although substantial psychiatric comorbidity was present in subjects meeting the criteria for MDD (more than 48% had comorbid anxiety disorder, for example), the proportion of patients with false-positive diagnoses of MDD with threshold-level psychiatric comorbidity was much lower: only 8 (23%) of the 34 met the criteria for generalized anxiety disorder and 4 others met the criteria for any other diagnosis (including 1 case of dysthymia). This was not significantly higher than the proportion of true negatives meeting the criteria for generalized anxiety disorder (15%).

So, in contrast to the Nijmegen results, we did not discover a large reservoir of threshold-level mental health disorders in our patients with false-positive diagnoses—including anxiety disorders, which might respond to the same treatment approach as depression. As noted in our original article, most patients with false-positive diagnoses of MDD (74% [25/34]) did have a history of mental health treatment and were known to their physicians as patients with previous episodes of depression. Furthermore, many would have met the criteria for subthreshold depression or anxiety at entry into the study. These results, considered together and in light of the Nijmegen findings described above, underscore one of the main conclusions of our study: DSM-IV diagnostic categories assigned on the basis of a single interview result in an inaccurate portrayal of mood disorder “caseness”—particularly along the depression-anxiety spectrum. Patients may meet the criteria for generalized anxiety disorder at one interview, meet the criteria for minor depression at another interview, then meet the criteria for full MDD with limited-symptom panic or somatoform disorder at a third interview. Do they have 3 separate disorders, or do they have 1 disorder of varying intensity and manifestations?

The issue is not whether DSM-IV–level precision in primary care diagnosis may be overstated, but whether DSM-IV represents a valid framework for mental health problems in primary care. The absence of longitudinal data describing the natural history of mood symptoms in primary care patients cripples our efforts to answer this question or to create a new model that more accurately captures the ebb and flow of symptoms, impairment, and response to treatment. The results of these and other cross-sectional studies can only highlight the need to return to basics: longitudinal clinical epidemiologic studies in this area.

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