Can Epidemiology Translate Into Understanding Major Depression With Borderline Personality Disorder?

Epidemiologic surveys have mapped the terrain of psychiatric disorders. Personality disorders have bedeviled the clinician's practice. Rarely have these two been rearranged in a meaningful clinical dialogue. Using the largest psychiatric epidemiologic survey ever, the National Epidemiologic Survey on Alcoholism and Related Conditions, and among the few to venture into axis II disorders, Skodol et al. (1), in this issue of the *Journal*, give a community-based national view of a common clinical question: What is the effect of specific personality disorder comorbidity on the course of major depression?

The original sample included over 40,000 adults, and 2,422 met criteria for DSM-IV current major depressive disorder. Three years later, 1,996 of the original currently depressed subjects were available for reinterviewing, which makes both a respectable sample size and response rate for generalizability. However, some caution is needed, since the sample was over-represented with Caucasian, college-educated, and married respondents. Fifteen percent of participants had persistent major depressive disorder, and 7.3% of those who remitted had a recurrence over the follow-up period. These figures are within the range of longitudinal studies of patients with major depressive disorder (2). While the presence of any personality disorder elevated the risk for persistence of major depressive disorder, when all axis I and II disorders, age of onset of major depressive disorder, number of previous episodes, family history, treatment, and duration of illness were controlled, borderline personality disorder remained the most robust predictor of major depressive disorder persistence. Neither personality disorders nor other clinical variables predicted recurrence of major depressive disorder. Thus, an epidemiologic survey yielded a practical jewel. The finding, undoubtedly, does not surprise the clinician but is now confirmed nationally. As the authors conclude, borderline personality disorder should be assessed in all depressed patients and considered in prognosis and addressed in treatment.

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One can raise a number of methodologic issues about this study, including the use of lay interviewers or the instrument for assessing axis II disorders. The diagnostic interview, the Alcohol Use Disorder and Associated Disabilities Interview Schedule, DSM-IV version (3), was developed for this survey. The personality disorders included were adapted from items in the Structured Clinical Interview for DSM-IV Personality Disorders. The test-retest and internal consistency results reported for all personality disorders are fair to good, not great. However, the agreement with clinician interviews for borderline personality disorder (kappa=0.71) is about as good as it gets (4). The only other national survey to venture into assessing all axis II disorders was the National Comorbidity Survey Replication (5), which used the International Personality Disorder Examination. The investigators carried out a clinical reappraisal in a sample of 214 subjects using clinically trained interviewers to follow up screened, positive subjects and reported excellent predictions of classification. They also noted that the International Personality Disorder Examination is commonly regarded as a conservative diagnostic

assessment of axis II disorders. The community rate they generated for any personality disorder in the United States was 11%, and in the World Health Organization World Mental Health Surveys (6), involving 13 countries, the rate was 6.1%. These rates seem to be lower than those reported in the National Epidemiologic Survey on Alcoholism and Related Conditions, but different presentations make it difficult to directly compare rates between studies. No articles from the National Epidemiologic Survey on Alcoholism and Related Conditions reporting overall rates of axis II disorders could be found. Unfortunately, given the findings in the Skodol et al. article, not all personality disorders were included in the first wave of the survey, and borderline personality disorder was added in the second wave. Both of these landmark studies used state-of-the-art measures. While they are imperfect, these are the best available. It is too bad they could not share the same methods.

The major issue now is not a debate about the *methods* of personality disorder assessment but about the *future* of personality disorders. The DSM-5 committee is working on the next version of psychiatric classification (7). In parallel, the National Institute of Mental Health is working on moving diagnosis away from clinical presentations to understanding of syndromes based on pathophysiology in a new project called Research Domain Criteria (8). These efforts will certainly effect how personality disorders are described, classified, or reimbursed in the future.

DSM-5 raises issues about the categorical conceptualization of personality disorders because of the high concurrence among disorders, both within and across axes, and the difficulty in differentiating normal from pathological. How dimensions will solve the problem of a lack of understanding of the pathophysiology underlying the disorders is unclear. Some cutoff along the dimension will need to be established for clinical practice.

The Skodol et al. study, based on an epidemiologic survey, may add light to the issue or, at least, generate a hypothesis about diagnosis that can be translated into a more experimental approach. Borderline personality disorder, defined categorically, and not the other axis II disorders explained the persistence of major depressive disorder over 3 years. Other axis I disorders may map out to different axis II disorders. The National Epidemiologic Survey on Alcoholism and Related Conditions, because of its large sample, could be mined for these clues about the relationship between specific axis I and II disorders.

The Research Domain Criteria project, in the long run, may offer more enlightenment for personality disorders if its goals can be achieved. The primary focus is on neural circuitry, with levels of analysis progressing from measures of circuitry function to clinically relevant variation or downward to the genetic and molecular cellular function (8). In the final analysis, the new molecular and neurobiological parameters will need to predict prognosis or treatment response. They will need to do as well as borderline personality disorder in predicting major depressive disorder persistence. If the Research Domain Criteria approach is successful, more than prediction of prognosis might be achieved, including a deeper understanding of the biological mechanism underlying the joined symptoms.

The epidemiologic finding that borderline personality disorder contributes to poor prognosis of major depressive disorder might be viewed as a hypothesis that can be translated into methods in the neurosciences to understand the mechanism behind this association. The features of borderline personality disorder, particularly the pervasive instability of the regulation of emotions and impulse control, would seem ripe for the Research Domain Criteria approach. When these symptoms occur in conjunction with major depressive disorder, a different syndrome may be present. Further experimental work may test how the symptoms of borderline personality disorder contribute to the prognosis of major depressive disorder. But what about the persistence of borderline personality disorder without major depressive disorder? Can the epidemiologic data provide any clues? In the meantime, the clinician treating major depressive disorder would be wise to assess for borderline personality disorder, even as currently defined.

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