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DSM-10: Coming Soon to a Psychiatric Practice Near You

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Two articles in this issue of the *Journal* focus on pediatric bipolar disorder (BD) and give us a taste of the future of psychiatric diagnosis.^{1,2} Specifically, these publications point the way toward our eventually being able to integrate symptom dimensions and biomarkers into clinical diagnosis, goals that have proved difficult to bring to fruition in *DSM-5* because of the limitations of our current knowledge.³ In this issue of the *Journal*, Axelson and colleagues¹ demonstrate the utility of applying a dimensional perspective to the diagnosis of BD in youth, and Bitter and colleagues² identify a potential biomarker for BD in adolescents (i.e., slow amygdala growth). It is no accident that these two informative articles are longitudinal, because longitudinal designs tend to mitigate the “noise” inherent in cross-sectional studies and, hence, are uniquely powerful in informing nosology.

Axelson and colleagues¹ examine a subgroup identified in the landmark Course of Bipolar Youth (COBY) study, i.e., those meeting the COBY definition for bipolar disorder not otherwise specified (BP-NOS). BP-NOS is a clinically important phenotype because it appears to be relatively common and severely impairing, and there are no studies to guide treatment.

In COBY, all youth assigned a BP diagnosis, including BP-NOS, must exhibit distinct episodes of hypomania and/or mania. An episode consists of a change in mood from baseline (i.e., irritability or euphoria that is unusual for that child) accompanied by the associated symptoms of mania, e.g., goal-directed activity, distractibility, grandiosity, etc. At the same time as the mood change, these associated symptoms must occur or exhibit a distinct worsening compared with that child’s baseline. It is these two simultaneous components—a distinct change in mood and the accompanying symptoms—that constitute an episode. In COBY, most youth with BP-NOS experience episodes that are too short to meet *DSM-IV* criteria for hypomania or mania (minimum of 4 or 7 days, respectively).

Axelson et al.¹ report on 140 COBY youth with BP-NOS followed for a mean of 5 years at a mean interval of 8.2 months. The main goal of the analysis was to identify the frequency and predictors of conversion from BP-NOS to *DSM-IV* BP type I or II. The rate of conversion was high: 23% converted to BP-I and 22% to BP-II. Regarding clinical characteristics at intake, the investigators tested several possible predictors of conversion (e.g., younger age, severe symptoms, history of major depression or hypomania), but only a history of BD in a first- or second-degree relative predicted conversion. Among subjects with BP-NOS and a positive family history, 58% converted compared with 36% without such a history. During the follow-up period, higher hypomania scores and intensive psychosocial treatment (but no

specific psychopharmacologic treatment) were associated with conversion; presumably, the latter was a result, not a cause, of the more severe symptoms.

What do these findings mean for the practitioner asked to assess a youth with BP-NOS? BP-NOS is not a benign condition and can be a harbinger of more frequent and severe symptoms to come. Aside from what BP-NOS predicts, many youth meeting BP-NOS criteria require treatment in the here and now; a previous publication reported that youth with BP-NOS had more symptomatic weeks than those with BP-I or II.⁴ Thus, the work of Axelson et al.¹ illustrates the importance of a dimensional approach, because we would know little about this phenotype—which is relatively common, can be impairing, and is associated with risk for future BD—if COBY included only youth with BP-I or BP-II and did not extend its work to youth with subsyndromal presentations along the “bipolar spectrum.”

At the same time, as we look toward future *DSMs*, work on BP-NOS illustrates some of the challenges we face in fully integrating a dimensional perspective into psychiatric practice. It is challenging to use dimensional data to inform treatment, because treatment is fundamentally a categorical decision or a series of categorical decisions; one decides to prescribe medication X or Y, psychotherapy A or B, neither, or both. Indeed, BP-NOS can be viewed as a category encompassing a broad range along the dimension of symptom frequency, spanning a spectrum that extends from youth with only a limited number of symptomatic hours in a lifetime to those with multiple 3-day episodes. In a trial of atypical antipsychotic medication or lithium in youth with BP-NOS, where along this broad spectrum should we place the categorical cutoff that defines who is eligible and who is not? Investigators studying individuals at “ultra-high risk” for schizophrenia have faced similar challenges when defining criteria for inclusion in clinical trials or for the conversion to psychosis.^{5,6} As we become more sophisticated about identifying disorders earlier in their developmental trajectory, we can expect to confront such issues across an ever-increasing number of illnesses.

Bitter et al.² point the way forward to another goal that we hope to see achieved in future editions of the *DSM*: the incorporation of bio-markers into the diagnostic process. In this important study, the investigators obtained structural magnetic resonance imaging scans in 30 adolescents hospitalized for their first episode of mania and then scanned the patients again approximately 1 year later. Two comparison groups, adolescents with attention-deficit/hyperactivity disorder (ADHD; $n = 29$) and healthy comparison subjects ($n = 24$), were also scanned twice at similar intervals. Left amygdala volume increased over time in patients with ADHD and healthy subjects, but not in those with BD. A similar pattern was seen in the right amygdala, although here the change over time in healthy subjects was not as marked. Exploratory analyses suggested that subjects with BD who achieved symptomatic recovery had a larger mean amygdala volume at baseline than those who did not. The longitudinal data in the study by Bitter et al.¹ are consistent with previous cross-sectional studies reporting smaller amygdala volumes in youth with BD than in controls.⁷

This study suggests that slow amygdala growth might be a biomarker for BD in adolescents and that, in adolescent mania, baseline amygdala volume might predict treatment response. Strengths of the study include a psychiatric comparison group (ADHD), which provides information about diagnostic specificity, and hand-traced amygdala volumes. Nonetheless, it is important for us to understand, and to reiterate to our patients, that we still have a long way to go before neuroimaging can be used to predict diagnosis or treatment response. The effect sizes of most neuroimaging findings are too small to translate into reliable differentiation between groups. Also, as Bitter et al.² note, we need considerably larger samples than in most current imaging studies to measure sensitivity and specificity. In

addition, unfortunately, it will be a major challenge to rule out the potentially confounding role of medication in findings such as those by Bitter et al.²

What do Bitter et al.² tell us about brain dysfunction mediating BD in adolescents? Prior data have indicated that ADHD, even when viewed dimensionally, is associated with an abnormally slow rate of cortical thinning.⁸ Thus, one could conclude that abnormal amygdala development characterizes BD but not ADHD and that abnormal cortical development characterizes ADHD (the extent to which aberrant cortical development also occurs in BD is unknown). Also, because the groups in the study by Bitter et al.² did not differ at baseline, the study highlights the importance of longitudinal research defining the developmental trajectory of an illness over time. As the development of these neural abnormalities is mapped, it will be important also to map the emergence of symptoms, neuropsychological deficits, and other measurements of aberrant behavior and cognition. In this way, neuroimaging data ultimately may shape clinical assessment by highlighting subtle behavioral and neural changes that may presage the development, or worsening, of psychopathology.

Thus, in this issue of the *Journal*, we have harbingers of the future. Axelson et al.¹ indicate how our current, largely categorical mode of diagnostic thinking will eventually be merged with a more dimensional perspective. Moreover, although a clinician's skill will always be the most important component of psychiatric diagnosis and care, Bitter et al.² hint at how biomarkers might eventually assist in diagnosis and treatment planning. Thus, from these two publications, we get a taste of *DSMs* to come.

References

1. Axelson D, Birmaher B, Strober M, et al. Course of subthreshold bipolar disorder in youth: Diagnostic progression from bipolar disorder not otherwise specified. *J Am Acad Child Adolesc Psychiatry*. 2011; 50:1001–1016. [PubMed: 21961775]
2. Bitter SM, Mille NP, Adler CM, et al. Progression of amygdala volumetric abnormalities in adolescents following their first manic episode. *J Am Acad Child Adolesc Psychiatry*. 2011; 50:1017–1026. [PubMed: 21961776]
3. Kupfer DJ, Regier DA. Neuroscience, clinical evidence, and the future of psychiatric classification in DSM-5. *Am J Psychiatry*. 2011; 36:672–674. [PubMed: 21724672]
4. Birmaher B, Axelson D, Goldstein B, et al. Four-year longitudinal course of children and adolescents with bipolar spectrum disorders: the Course and Outcome of Bipolar Youth (COBY) study. *Am J Psychiatry*. 2009; 166:795–804. [PubMed: 19448190]
5. McGorry PD, Nelson B, Amminger P, et al. Intervention in individuals at ultra-high risk for psychosis: a review and future directions. *J Clin Psychiatry*. 2009; 70:1206–1212. [PubMed: 19573499]
6. Yung AR, Nelson B, Thompson A, et al. The psychosis threshold in ultra high risk (prodromal) research: is it valid? *Schizophr Res*. 2010; 120:1–6. [PubMed: 20378314]
7. Pfeifer JC, Weige J, Strakowski SM, et al. Meta-analysis of amygdala volumes in children and adolescents with bipolar disorder. *J Am Acad Child Adolesc Psychiatry*. 2008; 47:1289–1298. [PubMed: 18827720]
8. Shaw P, Gilliam M, Liverpool M, et al. Cortical development in typically developing children with symptoms of hyperactivity and impulsivity: support for a dimensional view of attention deficit hyperactivity disorder. *Am J Psychiatry*. 2011; 168(2):143–51. [PubMed: 21159727]