Effects of Comorbid Anxiety Disorders on the Longitudinal Course of Pediatric Bipolar Disorders

Regina Sala, MD, PhD, Michael A. Strober, PhD, David A. Axelson, MD, Mary Kay Gill, MSN, Josefina Castro-Fornieles, MD, PhD, Tina R. Goldstein, PhD, Benjamin I. Goldstein, MD, PhD, Wonho Ha, PhD, Fangzi Liao, MS, Satish Iyengar, PhD, Shirley Yen, PhD, Heather Hower, MSW, Jeffrey Hunt, MD, Daniel P. Dickstein, MD, Neal D. Ryan, MD, Martin B. Keller, MD, Boris Birmaher, MD

Objective: To examine the longitudinal effects of comorbid anxiety disorders in youth with bipolar spectrum disorder (BP). **Method:** As part of the Course and Outcome of Bipolar Youth study, 413 youth, who were 7 through 17 years or age and who met criteria for *DSM-IV* BP-I (n = 244), BP-II (n = 28), and operationally defined bipolar disorder not otherwise specified (BP-NOS) (n = 141) were included. Subjects were followed on average 5 years using the Longitudinal Interval Follow-up Evaluation. Effects of anxiety on the time to mood recovery and recurrence and percentage of time with syndromal and subsyndromal mood symptomatology during the follow-up period were analyzed. **Results:** At intake and during the follow-up, 62% of youth with BP met criteria for at least 1 anxiety disorder. About 50% of the BP youth with anxiety had ≥2 anxiety disorders. Compared to BP youth without anxiety, those with anxiety had significantly more depressive recurrences and significantly longer median time to recovery. The effects of anxiety on recovery disappeared when the severity of depression at intake was taken into account. After adjusting for confounding factors, BP youth with anxiety, particularly those with ≥2 anxiety disorders, spent significantly less follow-up time asymptomatic and more time with syndromal mixed/cycling and subsyndromal depressive symptomatology compared to those without anxiety. **Conclusions:** Anxiety disorders are common and adversely affect the course of BP in youth, as characterized by more mood recurrences, longer time to recovery, less time euthymic, and more time in mixed/cycling and depressive episodes. Prompt recognition and the development of treatments for BP youth with anxiety are warranted. J. Am. Acad. Child Adolesc. Psychiatry, 2014;53(1):72–81.
Key Words: anxiety disorders, bipolar disorders, longitudinal study

The frequency with which anxiety symptoms accompany manic and depressive states was originally noted by Kraepelin,[1] and modern clinical and epidemiological studies also confirm the presence of anxiety disorders in youth with bipolar disorders (BP).[2-5]

Although comorbid anxiety disorders have been linked to poorer prognosis and an increased risk of suicide in youth with BP,[6] these observations are primarily cross-sectional in nature.[2,5] To our knowledge, only 2 studies have investigated the effect of comorbid anxiety disorders in youth with BP longitudinally. Masi *et al.*[7] followed a sample of 224 youth with BP spectrum disorders for a minimum of 6 months, noting that those with concurrent panic disorder (PD) showed less mood severity at baseline but greater persistence of illness during the follow-up compared to youth without PD. Similarly, DelBello *et al.*[4] followed a group of 71 adolescents with BP-I for 1 year after discharge from the hospital, and observed more severe mood symptoms and lower rates of recovery amongst adolescents with comorbid anxiety disorders compared to those without anxiety.

Clinical guidance is available at the end of this article.

Longitudinal studies in adults report similar associations: namely, that comorbid anxiety confers greater affective morbidity, including less

time spent with euthymic mood,[8-10] more severe depressive symptoms and more follow-up time in depression,[10,11] more rapid cycling,[8] increased time to episode remission,[8] and earlier relapse.[9] Comorbid anxiety has also been associated with greater substance use,[8] poorer psychosocial functioning,[8,9] and poorer response to pharmacological treatments.[10]

In a prior publication,[12] we reported that anxiety disorders that were ascertained at intake persisted in 50% of the youth with BP; persistence of anxiety disorders over the follow-up period was defined as at least 50% of follow-up time meeting full-threshold *DSM-IV* anxiety disorders criteria. Moreover, during approximately 5 years, 25% of the youth with BP who did not have anxiety disorders at intake developed new-onset anxiety disorders. In comparison to youth who had anxiety disorders at intake, youth who developed anxiety disorders during the follow-up showed significantly more substance abuse (10 of 92, 40%; versus 5 of 162, 33%; $\chi^2 = 6.4$, $p = .01$). There were no other between-group demographic or clinical differences. Given the clinical implications and the existence of few longitudinal studies examining the longitudinal effects of comorbid anxiety disorders in youth with BP, we sought to extend our prior findings and to examine the impact of anxiety on the 5-year prospective course and outcome of youth with bipolar spectrum disorders. Based on the literature, we hypothesized that, in comparison with BP youth without anxiety disorders, those with anxiety disorders would have less recovery and more recurrences, and a lower percentage of follow-up time spent asymptomatic, as well as more with syndromal and subsyndromal mood symptomatology.

METHOD

Subjects

The original sample of Course and Outcome of Bipolar Youth study (COBY) consisted of 446 youth (BP-I = 260, BP-II = 32, BP-NOS; n = 154). In comparison with the 413 who participated in this study, those who did not participate (n = 33) showed significantly less any anxiety disorders (39.2% versus 69.6%, $\chi^2 = 7.5$, $p = .006$). There were no other between-group demographic or clinical differences. The present study included 413 youth, aged 7 through 17 years 11 months (12.6 ± 3.3 years of age) who met criteria for Diagnostic and Statistical Manual IV (*DSM-IV*) BP-I (n = 244), BP-II (n = 28), and operationally defined BP-NOS (n = 141) and were recruited primarily through clinical referrals from 3 academic medical centers (University of Pittsburgh Medical Center, Brown University, and University of California at Los Angeles).[13] To date, subjects have been prospectively interviewed on average every 37.13 ± 20.4 weeks for a mean of 261.7 ± 94.1 weeks (~5 years). At present, the subject retention rate is 84.8%.

Because the *DSM-IV* criteria for BP-NOS are vague, the COBY study investigators set the minimum inclusion threshold for the BP-NOS group as subjects who did not meet the *DSM-IV* criteria for BP-I or BP-II but had a distinct period of abnormally elevated, expansive, or irritable mood plus the following: 2 *DSM-IV* manic symptoms (3 if the mood is irritability only) that were clearly associated with the onset of abnormal mood; a clear change in functioning; mood, and symptom duration of a minimum of 4 hours within a 24-hour period for a day to be considered meeting the diagnostic threshold, and a minimum of 4 days (not necessarily consecutive) meeting the mood, symptom, duration, and functional change criteria over the subject's lifetime, which could be two 2-day episodes, four 1-day episodes, or another variation.[14]

Institutional review board approval was obtained at each site before subject enrollment. After the institutional review board approval, consent or assent was obtained from all participants by project staff before study instruments were administered.

Procedures

The methods used to evaluate the subjects were reported in detail elsewhere.[15] In summary, at intake, children and parents were interviewed for the presence of current and lifetime psychiatric disorders using the Schedule for Affective Disorders and Schizophrenia for School Age Children, Present and Lifetime Version (K-SADS-PL),[16] the Kiddie Mania Rating Scale (K-MRS),[17] and the Depression Rating Scale (DRS), which was derived from the respective sections of the KSADS-P. The index episode was defined as the current or most recent episode assessed at intake. To ascertain the episode duration, time to recovery was calculated from the onset of the index episode. Therefore, for some subjects, the duration of episode exceeds the length of prospective follow-up.

Parents were also interviewed at intake about their personal psychiatric history using the Structured Clinical interview for *DSM-IV* Axis I Disorder (SCID),[18] and about first- and second-degree psychiatric family history using a modified version of the Family History Screen (FHS).[19] Socioeconomic status (SES) was measured using the Hollingshead 4-factor scale.[20] Functional impairment was assessed using the Child Global Assessment Scale (CGAS).[21] The child and parent Screen for Child Anxiety Related Emotional Disorder (SCARED)[22] was used to evaluate severity of anxiety symptoms. Pubertal status and equivalent Tanner

Download English Version:

https://daneshyari.com/en/article/324188

Download Persian Version:

https://daneshyari.com/article/324188

Daneshyari.com