Depressive Episodes and Symptoms Dominate the Longitudinal Course of Bipolar Disorder

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There is a new momentum to describe bipolar disorder in all its varieties and course patterns embracing a spectrum [1]. The authors' research group at the University of California, San Diego has been engaged in a series of investigations [2–5] of the long-term course of illness on a large cohort of patients with bipolar disorders (n=232; type I, n=146 and type II, n=86), who had been observed prospectively, longitudinally, and naturalistically for up to 20 consecutive years by the National Institute of Mental Health Collaborative Depression Study (CDS). The duration of the CDS and the detailed rigorous follow-up methods has provided a unique opportunity to analyze and describe the entire naturalistic symptomatic course of bipolar type I and bipolar type II *during* and *between* affective episodes. "Microanalysis" of all levels of severity of affective symptoms of the patients' weekly symptom status together with detailed analyses of all affective episodes, major and minor, has provided a more complete picture of the natural history of the illness over many years follow-up that is complementary to previous research efforts, which have focused primarily on the syndromal episode course of bipolar disorders. The authors have thereby uncovered several fundamental insights into the natural history of the longitudinal course of bipolar illness.

In this commentary, the authors wish to highlight characteristics of the long-term course of bipolar illness that previously had not been fully appreciated. The clinical and research focus in bipolar disorders has traditionally concentrated almost exclusively on explosive and disruptive episodes of mania and their management. As a result, the role of depressive episodes and depressive symptoms, including its treatment, has been relatively neglected. However, the authors' studies have demonstrated that the longitudinal expression of bipolar illness is dominated by depressive episodes and depressive symptoms. For example, patients with bipolar I experienced three times more depressive than manic symptoms during their longitudinal course of illness (*ie,* 31.9% of weeks with depressive symptoms; 9.3% of weeks with manic or hypomaniac symptoms, and 5.9% of weeks with cycling or mixed symptoms). The long-term course of bipolar II was dominated even more by depressive symptoms (50.9% of weeks), with patients experiencing very few follow-up weeks of hypomania or cycling or mixed affective symptoms (1.3% of weeks with hypomanic and 2.3% with mixed cycling symptoms; an approximately 30 to 1 ratio). The authors wish to point out, however, that what pertains to cycling or mixed states is based on the conservative criteria as they were described in 1978 in the Research Diagnostic Criteria.

When affective episodes were examined and compared between bipolar types I and II during the follow-up course, the findings were similar to those reported from the weekly analyses of the affective symptoms status. On average, a significantly higher percentage of bipolar type II patients experienced major depressive episodes compared with the bipolar type I patients during follow-up (type I=50% of patients, type II=74% of patients; P=0.009). In addition, patients with bipolar type II experienced significantly more follow-up weeks of acute minor depressive and chronic dysthymic states compared with that measured in patients with bipolar type I (type II mean=17.4% of weeks, type I mean=5.8% of weeks; P=0.001). Further, major and minor depressive episodes were treated significantly less often than manic or hypomanic episodes in patients with bipolar type I and type II during the course of illness.

In their naturalistic course, bipolar type I and type II are expressed longitudinally primarily by major and minor depressive episodes and subsyndromal depressive symptoms rather than manic or hypomanic episodes and subsyndromal hypomanic symptoms. Depressive episodes and symptoms predominated during the long-term longitudinal follow-up of bipolar type I and type II, however, it is type II that was overwhelmingly depressive in nature. Bipolar type II then represents the depressive pole of the bipolar spectrum, with the rare recurrent mania at the other end of the spectrum.

The authors submit that the longitudinal weekly course of bipolar type I and type II primarily involves depressive and not manic or hypomanic symptoms. Patients with bipolar type I experienced weeks of depressive symptoms approximately three times more often than manic or hypomanic symptoms. Strikingly, bipolar type II patients experienced weekly depressive symptoms over 30 times more commonly than weeks of hypomanic or subsyndromal hypomanic symptoms. Depressive episodes, major and minor, played a substantial role in the lifetime course of bipolar type I and type II. As with the symptomatic analyses, when affective episodes were also analyzed, although bipolar type I and type II had approximately the same mean number of major depressive episodes, significantly more patients with bipolar type II experienced episodes of acute minor depression and dysthymia (chronic minor depression). Thus, bipolar type I and type II are expressed primarily by depressive symptoms in their longitudinal course.

The authors wish to offer a caveat that patients with bipolar often lack insight during the manic and especially, the hypomanic episodes, and they often experience their condition as normal. Thus, perhaps, those with frequent mania or hypomania are less likely retained in a longitudinal cohort. The authors' studies nonetheless point out that the depressive expression of bipolarity will present most often to the clinician. The dominance of depressive symptoms has been also confirmed in epidemiologic community samples. The lifetime prevalence figure of 0.8% that was originally reported by the Epidemiological Catchment Area study for the predominantly manic forms of the illness [6] has been boosted to 6.4% in the authors' re-analyses [7] of the manic and depressive aspects of bipolarity in this same Epidemiological Catchment Area sample. In other words, major and minor depressive episodes, hypomania, mania, as well as subsyndromal affective symptoms, all of which represent the full affective components of the bipolar spectrum, were included in this analysis. Similar data have emerged from the Zurich Epidemiologic Project [8].

It is of paramount significance for psychiatrists to recognize the ubiquity of the depressive phase of bipolar disorder and focus on its treatment. The research community is also urged to increase its focus on the role of depression in bipolar illness. These data and considerations are of immense importance for the new public health agenda of bipolar disorder.

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