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BIPOLAR DISORDERS (W CORYELL, SECTION EDITOR)

Problems in the Boundaries of Bipolar Disorders

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Abstract Classical concepts of bipolarity (bipolar I and bipolar II) have sometimes been extended into a broader spectrum that includes a wide variety of conditions previously diagnosed as separate forms of psychopathology. Differential diagnosis remains important, particularly in personality disorders characterized by affective instability, and in behavior disorders affecting pre-pubertal children. In the absence of biological markers or other external sources of validity, as well as lack of evidence for response to pharmacological treatment when disorders are defined more broadly, the bipolar spectrum remains an unproven hypothesis.

Keywords Bipolar disorders · Bipolar-II disorder · Bipolar spectrum · Affective instability · Personality disorders · Pediatric bipolar disorder

Introduction

Bipolar disorder is a major mental illness that has attracted a very large body of research. Its classical forms, bipolar-I and bipolar-II disorders, have unmistakable clinical features, and their validity is supported by a broad literature [1]. However, in its plural form, the term "bipolar disorders" has been used to describe variants of these classical clinical pictures, as well as conditions that may be diagnostically distinct [2]. The concept of a bipolar spectrum [3, 4] needs to be supported by biological markers and/or by evidence that treatments known to be effective for the classical forms are also effective for spectrum conditions.

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Classical Bipolarity

Kraepelin [5] was the first to distinguish schizophrenia, a chronic disease affecting cognition, with a poor prognosis, from bipolar disorder, an episodic condition mainly affecting mood, with a better prognosis. However, this dichotomy has been challenged, particularly by research suggesting that genetic vulnerability to psychosis is common to both [6]. In clinical practice, most patients can be placed on or the other side of the divide. However, when psychiatrists are not sure, they may use the category of schizo-affective disorder, which was retained in DSM-5 [7]. A recent review concluded that many patients with that diagnosis have a more severe form of bipolar disorder [8], in which psychotic features are particularly prominent, leading clinicians to question a diagnosis of primary mood disorder.

Bipolar-II disorder was a new category in DSM-IV [9]. While this condition is marked more by depression than by hypomania [10], most researchers have considered it to be a less severe variant of bipolar I [11]. Also, while characterized by hypomania instead of full mania, its symptoms may also respond to lithium [12, 13]. However, making this diagnosis requires a careful assessment of mood symptoms. The most important principle is the requirement in DSM-5 [7] that hypomania last for at least 4 consecutive days and abnormal mood be continuous. Bipolar II cannot be diagnosed only on the basis of an unstable mood, particularly when mood swings last only for an hour or two.

Another question about bipolar II is whether it describes a specific form of psychopathology or whether it is a heterogeneous category. Some researchers have suggested it takes two forms, one closer to classical bipolarity and another presenting

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more ”characterological” features [13]. But if one applies the criteria for hypomania strictly, only the first type would be a form of bipolar disorder.

Another concept that has extended the reach of classical bipolarity is the hypothesis of an occult form presenting with depression only, suggesting that patients with treatment-resistant depressions may be unresponsive to drugs because they have an underlying bipolar disorder [14]. It is true that some patients with unipolar depression become bipolar over time, particularly if a depressive illness is severe enough to require hospitalization [15] or if it is highly treatment resistant [16]. However, it does not follow that occult bipolarity should be routinely suspected in unipolar cases, particularly when depressive symptoms are mild to moderate.

The Bipolar Spectrum

The expansion of bipolarity into a broader spectrum can lead to a very wide prevalence of such conditions. A survey in a large clinical sample using broad criteria for the spectrum [17] identified bipolarity in 40 % of *all* outpatients. However, these diagnoses were based almost entirely on instability of mood, not on the presence of hypomania. Validity of the spectrum therefore depended on a circular argument. External validators would be needed to prove that these subclinical phenomena actually indicate the presence of bipolarity.

The concept of a bipolar spectrum assumes that a wide range of patients receiving other diagnoses “really” suffer from a milder (or variant) form of bipolar disorder. The list of conditions that have been considered to lie within the spectrum includes treatment-resistant major depression, substance abuse, and personality disorders [3]. To support this hypothesis, we would need an understanding of the endophenotypes behind bipolarity, as well as an ability to identify biomarkers associated with these processes. In their absence, evidence for the concept mainly depends on symptoms and family history data, which are subject to interpretation and not fully objective.

Patients who do not meet criteria for hypomania cannot be considered to have bipolar II. However, DSM-5 allows for a broader diagnosis if one uses the category bipolar disorder, unspecified [7]. That condition is not well studied, and it is not known how often it is applied in practice. Even so, this category allows clinicians to diagnose bipolarity in the absence of any classical features and can be used to describe any patient with mood swings as having a form of bipolar disorder. Like most of the residual categories in the manual, its validity is unknown.

Identifying hypomania would be more reliable if clinicians took the time to question key informants about the patient’s symptoms [18]. To identify a hypomanic episode in a patient, global impressions are not sufficient. One needs to establish duration, whether mood was consistent or inconsistent, and whether any of the characteristic hypomanic symptoms (rapid speech, little need to sleep, excessive spending, and grandiose plans) were present, as well as whether other people noticed them. Doing so usually requires direct interviews of family members and intimates.

Similar cautions apply to recognizing bipolar symptoms in first-degree relatives [18]. Even in research, it is rare for reports of family history to be confirmed by informants, and one cannot assume that diagnoses made on unseen relatives are valid. The danger is that histories of moodiness will be deemed sufficient, in and of themselves, to support a positive family history. Stronger evidence would be provided by a history of hospitalization or multiple hospitalizations for manic episodes.

If one considers bipolar II to be only one of several variants of the classical illness, diagnosis will be more frequent. Some researchers [19] have suggested creating new categories to delineate a broader spectrum (bipolar III for antidepressant-induced hypomania, bipolar IV for ultra-rapid mood swings). These ideas were not incorporated into DSM-5, but tend to suggest a more aggressive psychopharmacological approach.

The main reason for expanding the bipolar spectrum may be related to a wish to treat difficult patients with effective medication. However, no randomized clinical trials show that psychopharmacological interventions known to be effective for bipolar I and bipolar II are also effective for spectrum disorders [20]. In the absence of such evidence, caution about making such diagnoses may be the best course.

Affective Instability and Bipolarity

Affective instability (AI) is a trait that shares features with trait neuroticism, but is distinct in that it describes not just extreme emotional sensitivity, but also temporal instability [21]. AI is one of the main characteristics of borderline personality disorder (BPD) and is usually associated with high levels of impulsivity [22, 23]. These patients have rapid shifts of mood in response to life circumstances, usually in response to interpersonal triggers, and unstable mood that can shift by the hour, usually from depression to anger and irritability [24–26]. Due to a failure to observe the time scale for hypomania, BPD patients are frequently diagnosed as bipolar [27, 28].

Affective instability (AI) may be a separate phenomenon from bipolarity, derived from a distinct endophenotype. Several lines of investigation support this conclusion. There are major differences in phenomenology between AI and hypomania [26]. Moreover, researchers have examined the precipitants for mood swings using ecological momentary assessment (a method of monitoring social interactions in vivo). These studies have shown that rapid mood swings in BPD

are not spontaneous, but a response to negative social interactions, and that they usually involve anger, not elation [29–31].

Another important line of evidence is that AI in BPD is accompanied by impulsive actions that are not typical of bipolar disorder, such as self-harm [23]. BPD patients also suffer from notable instability in intimate relationships [23], and these interpersonal problems are also not typical of bipolar disorder. Also, only a minority of patients with BPD (estimated in one study as 3.8 %) [32] ever develop hypomanic episodes. When that does happen, the personality disorder diagnosis should be questioned. Finally, longitudinal follow-up of BPD shows that unstable mood is its most stable clinical feature, even when other symptoms remit [33, 34].

When patients with BPD are viewed as bipolar because of mood swings, they may receive drugs for which evidence for effectiveness is weak [35]. Mood stabilizers and antipsychotics can provide short-term symptomatic relief [36]. But in contrast to the powerful and convincing effects in classic bipolar illness, they *never* yield a full remission of BPD, and a recent Cochrane report did not find strong enough evidence to recommend their use [35].

Ironically, although bipolar disorder tends to be seen as more treatable, its prognosis is worse. While bipolar disorder often continues into old age [1], longitudinal studies show that BPD usually improves as patients approach middle age [33, 34].

Although there are no biological markers for personality disorders, family history studies [37] show that the first-degree relatives of patients with BPD are most likely to have substance abuse and personality disorders, not bipolarity. Behavioral genetic studies show that traits underlying personality disorders are heritable, but do not overlap with bipolarity [38]. Neurobiological studies also support the conclusion that bipolar disorder and BPD derive from separate endophenotypes [39]. Studies of the childhood precursors of BPD [40] show that this form of pathology begins with behavioral disorders prior to puberty, and not with mood disorders. There is little evidence that BPD and bipolar disorders share etiological factors, phenomenology, or treatment responses [41, 42].

In summary, patients with affective instability without hypomania are more likely to suffer from a personality disorder than from a bipolar disorder. Research does not support the claim that BPD is nothing but a subclinical form of bipolarity and that other disorders with impulsive patterns, such as substance abuse, are also forms of bipolarity, and should be treated in the same way [3].

Pediatric Bipolar Disorder

The most controversial expansion of the bipolar spectrum has been the idea that bipolar disorder can be diagnosed in pre-pubertal children. Since the time of Kraepelin [5], it has been generally accepted that bipolar disorder rarely appears before adolescence. The evidence base for making bipolar spectrum diagnoses in young children is based on similar assumptions as have been applied to adults. Children do not develop hypomania, but can show affective instability, usually associated with behavioral dyscontrol and impulsivity. One research group that followed a group of these children into adolescence found that patients remained affectively unstable and were prone to depression [43]. Another study [44] that claimed to find continuity of bipolarity from childhood to adolescence used methods that failed to distinguish whether cases fell within a spectrum or had classical forms of bipolar disorder.

When children are seen as bipolar, they tend to be prescribed the same drugs used in adults, particularly with antipsychotics. This trend has been documented in practice surveys [45], has not been supported by clinical trials [46•], and has also aroused opposition and concern. DSM-5 [7] therefore decided to introduce a new category, disruptive mood dysregulation disorder, specifically aimed to avoid diagnosing young children as bipolar. At this point, this novel diagnosis requires much more research [47].

Conclusions

Evidence for a bipolar spectrum remains weak and must be considered as a hypothesis with insufficient support to be applied to clinical practice. Adoption of this concept in research has been used to claim that there is a very high community prevalence of bipolar spectrum disorders [48], but everything depends on how these conditions are defined. The boundaries of bipolar disorder remain problematic, particularly at the interface with personality disorders [49•]. There are, for example, important clinical differences between bipolar-II depression and BPD [50]. In contrast, there is more evidence supporting the classical Kraepelinian distinction between bipolar I and schizophrenia [51•].

Instead of extending treatment to patients viewed as falling within a spectrum, psychiatrists might be better advised to focus their efforts on bipolar-I and bipolar-II disorders, which present sufficient clinical problems. For example, bipolar I has a more serious course than Kraepelin described, and bipolar-II disorder can be problematic, particularly when the clinical picture is dominated by depression [11]. If half the effort that has gone into studying the bipolar spectrum were devoted to developing new and better methods to manage

those with classical forms of this disorder, patients might gain more benefit.

Compliance with Ethics Guidelines

Conflict of Interest Joel Paris declares that he has no conflict of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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