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Bipolar and Related Disorders

Bipolar Disorders in DSM-5

Kraepelin was the first psychiatrist to systematically describe manic-depressive illness. Later, another German, Karl Leonhard (1979), suggested a name change to *bipolar disorder*, distinguishing between cases of mood disorder presenting with depressive episodes (unipolar) and those that swing from depression to mania (bipolar). Eventually, bipolar disorder itself was divided into two types, one with full mania (bipolar I) and the other with hypomania (bipolar II; Parker, 2012).

The criteria for bipolar I disorder have not been changed in the new manual. The patient must meet criteria for a manic episode, and the clinician must specify whether there are psychotic features, mixed features, catatonic features, rapid cycling, anxiety, suicide risk, a seasonal pattern, or a postpartum onset. For bipolar II disorder, there must have been a hypomanic episode, as well as a history of major depressive episodes, and symptoms must be clinically significant.

Bipolar I disorder with classical manic episodes is one of the best-defined illnesses in the DSM manual. Even so, there are problems with its boundaries. The category of schizoaffective disorder allows clinicians to fudge the question as to whether a patient has schizophrenia or a mood disorder. Years ago, Pope and Lipinski (1978) showed that most of these cases can be placed in bipolar disorder or schizophrenia by taking a careful family history and examining treatment response. Later, Lake and Hurwitz (2006)

concluded that most schizoaffective patients have a mood disorder and are simply showing more severe psychotic features than clinicians expect. But this diagnosis is also sometimes used to describe schizophrenic patients who are depressed. Contrary to clinical lore, schizophrenia is not necessarily associated with flattened affect; many patients are understandably depressed about living with a disabling mental disorder (Andreasen, 1979). DSM-5 might have removed the schizoaffective category entirely, but it chose not to do so.

The other disorders described in this chapter of DSM-5 are rare. Cyclothymic disorder describes subthreshold hypomanic and depressive symptoms over a 2-year course. Unspecified bipolar disorder (previously bipolar NOS) is rarely used, but it could become common if clinicians choose to diagnose the disorder even when symptoms do not meet the threshold for either bipolar I or bipolar II. As we will see, the research literature is replete with studies that call such cases "bipolar II" (despite the absence of hypomania), consistent with the concept of a bipolar spectrum.

The Overdiagnosis of Bipolar Disorder

In the past, bipolar disorder was underdiagnosed and was often confused with schizophrenia. Forty years ago, the use of lithium for the acute treatment of mania, and for the prevention of relapse, changed everything. These results led psychiatrists to wonder if they might achieve the same results in other patients by reconsidering whether they actually suffer from a form of bipolar disorder. Schizophrenia was the first target for rediagnosis. For example, abnormal states of excitement previously categorized as catatonic schizophrenia could be redefined as forms of mania. "First-rank" symptoms of schizophrenia—such as thought broadcasting and thought insertion, long thought to be pathognomonic of schizophrenia—turned out to be common in manic patients (Abrams & Taylor, 1981). The most convincing evidence for changes in diagnosis was the

observation that some patients previously diagnosed with schizophrenia could be treated successfully with lithium.

Because lithium, unlike antipsychotics, also did a good job of preventing relapses of mania in the long term, psychiatrists were keen to use it, and many more psychotic patients began to be diagnosed with bipolar disorder (Paris, 2009). But this change in practice had problems. Rediagnosis could be right or wrong, but there was no way of telling. Most clinicians looked to see whether patients got better on lithium. But it is often difficult to determine whether a patient has responded to this drug given that bipolar disorder is episodic and that lithium is often prescribed during a hospital admission—at the same time as numerous other interventions. The diagnosis usually becomes clearer when patients are followed over time.

There has been much controversy about the boundaries of bipolar II (Parker, 2012). The introduction of this category in DSM-IV, with mood swinging from depression to hypomania, was a good decision, but bipolar II has become too popular for its own good. We have seen a diagnostic epidemic largely because of a preference for identifying conditions that can be managed with drugs. It has also opened the door to a major expansion of the bipolar diagnosis so that all phenomena marked by mood instability can be seen as reflecting milder forms of bipolarity on a spectrum. Bipolarity came to be defined in ways that expand into the boundaries of other mental disorders, and some have claimed it is present in a large percentage of patients who see psychiatrists (Akiskal et al., 2006). Strict observance of criteria would lead these cases to be diagnosed as bipolar NOS (or, in DSM-5, "unspecified").

Kraepelin (1921) suggested that milder forms of mania can develop in the absence of classical symptoms. But he probably would have been surprised to see physicians diagnosing bipolar disorder in 5–10% of the general population. In recent years, any and all forms of mood swings or unstable mood have been proposed to lie on a spectrum (Akiskal, 2002; Angst & Gamma, 2002). This tendency to view mood disorders, personality disorders, and impulsive disorders as "bipolar" has spread rapidly. It has even entered common

parlance. Also, the concept has been expanded to include an even broader group of clinical problems.

The leaders of the bipolar spectrum movement have been American psychiatrist Hagop Akiskal (2002) and Swiss psychiatrist Jules Angst (1998), supported by several other prominent researchers (Ghaemi et al., 2002; Goodwin & Jamison, 2008;). All state that bipolarity is underdiagnosed and much more prevalent than previously believed. In light of their suggestion that up to 40% of all psychiatric patients suffer from variants of this condition, I have described them as "bipolar imperialists" (Paris, 2009).

To explain this critique, let us return to the traditional definition of mania based on a "triad" of signs and symptoms: elevated affect, psychomotor excitement, and racing thoughts. Classically, psychiatrists did not diagnose mania in the absence of euphoria. However, soon after the introduction of lithium, it was observed that bipolar I patients can show irritability rather than elevated mood and that this symptom can also respond to mood stabilizers (Winokur & Tsuang, 1975). That observation led some to question whether states of excitement, irritability, and aggression seen in other categories of mental disorder could be symptoms of mania and whether the classical triad is a necessary condition for bipolarity. The clinical situation was further modified by the concept of a "mixed episode," a poorly researched category in which patients are both depressed and irritable. (This clinical picture might correspond to what used to be called "agitated depression.") In DSM-5, such episodes are a specifier rather than a separate diagnosis.

The key issue in making a bipolar II diagnosis is to ensure that patients meet criteria for hypomania. These episodes have very specific requirements related to timescale and persistence. A hypomanic episode, as defined in DSM-IV-TR, consisted of "persistently elevated, expansive, or irritable mood, lasting throughout at least 4 days." If not directly observed, the assessment of hypomania by retrospective patient report is difficult because one cannot readily determine whether mood elevation was persistent or how long it lasted (Dunner & Tay, 1993). You often need to interview key informants to be sure. Briefer periods of elevated mood that do not

persist describe mood instability but do not meet formal criteria for hypomania. They can also be produced by substance use, particularly with stimulants, or personality disorders.

We need to distinguish putative spectrum disorders from bipolar II. Admittedly, the DSM-IV requirement that elated or irritable mood be present continuously for at least 4 days is arbitrary. But a shorter period would be equally arbitrary. One could dimensionalize hypomania so that symptoms for the full 4 days would not even be required. But scale and timing are often used in medicine to determine boundaries between pathology and normality. Before introducing a spectrum concept that would lead to major changes in diagnosis, we should know whether all mood swings share a psychopathological mechanism.

Many patients with personality disorders have mood swings lasting for only an hour or so. Clinical assessment has to be done carefully to determine that hypomania has been continuous and does not produce the "roller coaster" mood described by people suffering from borderline personality disorder. Regarding the length of hypomania, 4 days is on the low side, and because most episodes are longer, this should be considered a minimum. Moreover, because most information about hypomania is collected retrospectively, it is often difficult to be sure that abnormal mood has persisted without respite for the entire period. Even more important, mood swings that are primarily subjective and do not lead to changes in behavior that other people are almost sure to notice (e.g., rapid speech, little need for sleep, and overspending) do not constitute hypomania.

Even so, Benazzi (2004) and Angst (1998) recommended that 1 or 2 days of continuously feeling "high" is sufficient to identify hypomania. These researchers view diagnosis as depending more on family history. Yet that procedure is slippery because it may be based only on a patient's report (as opposed to direct interviews of family members), sometimes only indicating that a first-degree relative had some form of unstable mood. I do not disagree that bipolar disorder can begin with subclinical symptoms. Moreover, not *all* patients with unstable mood will eventually develop a classical bipolar disorder. This is the same problem we saw with attenuated psychosis syndrome: It produces too many false positives.

Lowering the bar would inevitably lead to a huge increase in diagnosis of bipolarity—this has already happened. Few clinicians observe the 4-day rule, and some respond with a "bipolar" knee jerk to mood swings of any kind. The result is the prescription of mood stabilizers and antipsychotics to patients who may or may not need them.

In the end, DSM-5 did not modify the 4-day rule. The workgroup concluded that the evidence was not strong enough to do so and that the consequences would be unpredictable. This was a reassuringly sensible decision.

Ghaemi et al. (2002) proposed a category of "bipolar III" to describe hypomania brought on by antidepressants. DSM-IV did not consider this a separate syndrome but, rather, the effect of a drug. In DSM-5, episodes of mania or hypomania that follow treatment with antidepressants are classified in the same way as other cases—assuming they continue well beyond the pharmacological intervention.

It turns out that the scenario of a shift to hypomania after antidepressant therapy is not common (Parker & Parker, 2003). Confusion arises because bipolar disorder often emerges from an initial depression, and the switch can be independent of drug treatment. Interpreting the emergence of mania as *caused* by an antidepressant, rather than as an evolution of a disease process, can be illusory. This makes it doubtful whether we need a diagnosis of bipolar III.

Ghaemi et al. (2002) also proposed adding a category of bipolar IV to describe ultra-rapid mood swings, even those that last only for a few hours. These clinical phenomena, better described as affective instability, may not be a form of bipolarity at all and are characteristic of patients with borderline personality disorder (Koenigsberg, 2010). Bipolar imperialists do not, however, believe in the existence of that condition, which is seen as a bipolar variant.

The use of the term "ultra-rapid" conflates rapid-cycling bipolar illness, defined by frequently recurring episodes of mania or hypomania, with mood that changes from day to day or from hour to hour. Affective instability—that is, brief mood changes

characterized by temporal instability, high intensity, and delayed recovery from dysphoric states—could well be an entirely different psychopathological phenomenon. Without biological markers, how can we know?

Once ultra-rapid mood swings are admitted as diagnostic criteria, many other mental disorders can fall within the bipolar spectrum. Again, the concept depends entirely on phenomenological resemblances that are observable but ultimately superficial. We should not conclude that common symptoms necessarily reflect similar underlying disease processes. Mood instability is a common symptom in personality disorders, substance abuse disorders, and eating disorders. Akiskal (2002) takes this as evidence that *all* of these patients are "really" bipolar. Making affective instability equivalent to bipolarity also led some child psychiatrists (e.g., Chang, 2007) to redefine many of the common behavior disorders of childhood as "pediatric bipolar disorder." This issue will be discussed separately later.

Definitional problems have also affected estimates of how common bipolar disorder is in the community. In the Epidemiological Catchment Area study (Robins & Regier, 1991), the lifetime prevalence of bipolar I was 0.8%, and that of bipolar II was 0.5%. These were conservative and believable numbers. But in the National Comorbidity Survey (Kessler et al., 1995), the lifetime prevalence of bipolar I increased to 1.6%. Then, the National Comorbidity Study Replication reported the combined prevalence for bipolar I and bipolar II to be 3.9% (Kessler et al., 2005a), an increase that directly followed from a broader concept of hypomania. All these numbers were based on DSM-IV criteria. When "subclinical" symptoms such as mood instability and irritability were assessed with an instrument to determine the frequency of bipolar spectrum disorders (Merikangas et al., 2007), bipolar I was estimated to have a prevalence of 1%, bipolar II increased to 1.1% (a notable increase), and subthreshold cases added an additional 2.4% for a total of 4.5%.

Depending on how much one broadens the spectrum, community prevalence could be much higher: Angst (1998) suggested an

estimate of 8%—twice the most elevated numbers. In clinical samples, in which protocols can be designed to identify spectrum symptoms using dimensional "indexes" of bipolarity, prevalence can be even more dramatically elevated. For example, 39% of *all* patients in a large study of patients at multiple sites in France were reported to have experienced episodes of broadly defined hypomania (Akiskal et al., 2006).

The problem is the absence of a gold standard. The psychiatrists who want to expand DSM criteria conduct research using scales designed to measure what they call "soft bipolarity" (Perugi & Akiskal, 2002)—that is, spectrum cases defined by putative subthreshold symptoms. But how do we know that these symptoms are true indicators of bipolarity? Phenomenological resemblances are not sufficient. It is possible that subclinical symptoms of moodiness reflect a different type of psychopathology—or normal variations not related to mood disorders.

The concept of a bipolar spectrum stands on firmer ground when applied to recurrent unipolar depression. Here, we can have a problem with *underdiagnosis* of bipolarity. Kraepelin (1921) was the first to observe that severe depression can develop over time into bipolar disorder. This outcome is more likely to occur in the presence of an early onset, a recurrent course, atypical symptomatology, and a family history of bipolarity (Benazzi, 2002).

Every practitioner will have seen such cases. But the frequency of latent bipolarity in outpatient practice or primary care has been greatly exaggerated. As the concept became popularized, I received many consultations from family doctors asking if patients with *mild to moderate* depression, and who had not responded to drug therapy, were "really bipolar." Patients, who can be attracted to faddish diagnoses, may also adopt this viewpoint, breezily stating that they (or their relatives and friends) are bipolar. Expanding the spectrum has also been supported by the media (which like a simple story) and by the pharmaceutical industry (which is searching for a larger market).

The promoters of the bipolar spectrum are sincere but misguided. They are promoting models that lead to a large number of

false-positive diagnoses. They want to rediagnose a large number of patients and put them on mood stabilizers and/or antipsychotics. A broad bipolar spectrum would certainly take up a very large chunk of psychiatry, but the fad is more based on enthusiasm than on evidence.

One way to validate diagnoses is by identifying a characteristic treatment response. The concept of "pharmacological dissection" is based on evidence that the same agent can produce the same effect in patients who fall in different categories (Klein, 1987). Although classical bipolar disorder usually responds to mood stabilizers, we lack randomized clinical trials to show whether these drugs work in the same way in spectrum disorders, and the evidence suggests they do not (Paris, 2012). Patients with putative bipolarity do not consistently respond to the pharmacotherapy that works in classical cases (Patten & Paris, 2008).

For example, in patients with personality disorders associated with affective instability, the evidence for using *any* drug for these populations is weak (Kendall et al., 2009; Paris, 2008c), and mood stabilizers are not specifically effective. Confusion arises because psychiatric drugs can have broad sedative effects that reduce the frequency of all kinds of problematic symptoms and behaviors. No one would claim that relief from pain obtained by prescribing analgesics proves that all patients who respond to them have the same illness.

Pediatric Bipolar Disorder

In recent years, controversy has arisen as to whether bipolarity can be diagnosed in prepubertal children. Since the time of Kraepelin (1921), it had been generally accepted that bipolar disorder rarely begins before adolescence. And although no one disagrees that classical bipolarity can be seen soon after puberty, the concept of a bipolar spectrum has led clinicians to diagnose it in adolescents who would be better described as having a personality disorder (Chanen et al., 2008). There has also been confusion about

definitions because for some, "childhood" means before 18 years of age, whereas for others it means before adolescence.

The concept that mania can begin in childhood and is actually common before puberty has become influential (Faedda et al., 2004; Wozniak, 2005). Frances (2010f), who views pediatric bipolar disorder as an example of a diagnostic fad, comments,

> To become a fad, a psychiatric diagnosis requires three preconditions: a pressing need, an engaging story, and influential prophets. The pressing need arises from the fact that disturbed and disturbing kids are very often encountered in clinical, school, and correctional settings. They suffer and cause suffering to those around them—making themselves noticeable to families, doctors, and teachers. Everyone feels enormous pressure to do something. Previous diagnoses (especially conduct or oppositional disorder) provided little hope and no call to action. In contrast, a diagnosis of childhood bipolar disorder creates a justification for medication and for expanded school services. The medications have broad and nonspecific effects that are often helpful in reducing anger, even if the diagnosis is inaccurate.

What is actually observed in so-called "bipolar children"? If you read the research reports carefully, they describe a broad and persistent emotional dysregulation (Birmaher et al., 2009; Geller et al., 2008). Although these children have mood swings, they do not develop manic or hypomanic episodes. They are moody, irritable, oppositional, and likely to misbehave—like all children with disruptive behavior disorders. Their grandiose thinking consists of little beyond boastfulness.

No evidence from genetics, neurobiology, follow-up studies, or treatment response shows that this syndrome has anything in common with classical bipolarity. In a prospective study of children of bipolar parents (Duffy., 2007), mood disorder episodes (mostly depression) started only after puberty, and no features of bipolarity were observed in the cohort prior to that. Another prospective study found that children of bipolar parents are at risk for

attention-deficit hyperactivity disorder (ADHD) rather than bipolarity (Birmaher et al., 2010).

Some of the most interesting findings come from follow-up studies of a group of children in St. Louis who received a bipolar diagnosis (Geller et al., 2008). Yet the research group did *not* find that the syndrome evolves into bipolar disorder in adolescence, and others have also failed to find such a relationship (Birmaher & Axelson, 2006). Even though the clinical picture can persist over years (Geller et al., 2002), it remains at the level of "soft bipolarity." Although these children show moodiness and irritability, they do not have hypomanic episodes. In the end, symptoms considered to be "bipolar" in adults need not have the same meaning in children. Moodiness and disruptive behavior are very common among children studied in community surveys (Duffy, 2007). They are also among the most frequent symptoms in children referred to psychiatrists.

Brotman et al. (2006) introduced a different term to describe such cases: *severe mood dysregulation* (SMD). They also found that children with this picture go on to develop depression—*not* mania—later in life. Similar conclusions have been reached by other researchers (Carlson, 2011; Leibenluft, 2011).

DSM-5 at one point suggested using the term "temper dysregulation disorder," but because that diagnosis could be confused with temper tantrums, it was replaced by *disruptive mood dysregulation disorder* (DMDD). This terminology views the syndrome as a variant of a mood disorder and not as a classical behavior disorder such as conduct disorder or oppositional defiant disorder. The main purpose of this new terminology could be to discourage an automatic prescription of mood stabilizers and antipsychotics. However, the wish to prescribe drugs to seriously disturbed children does not only depend on diagnosis. Most clinicians would not be surprised if children with DMDD routinely receive antipsychotics.

Copeland et al. (2013) studied DMDD using data from three large community studies. The diagnosis was common (0.8–3.3%), but most cases were comorbid with depression or oppositional defiant disorder. These findings raise questions about the specificity of a diagnosis that seems to have been brought into DSM-5 to offer

clinicians an alternative to "pediatric bipolar disorder." In any case, bipolar disorder before puberty also has a large overlap with other diagnoses. Geller et al. (2008) observed particularly strong comorbidity with disruptive behavioral disorders (conduct disorder, oppositional defiant disorder, and ADHD). None of those conditions are precursors of adult bipolarity. Long-term studies following children with ADHD into adulthood (Manuzza and Klein, 2000; Weiss & Hechtman, 1993), as well as of children with conduct disorder (Zoccolillo et al., 1992), show an increased risk for developing antisocial personality disorder and substance use but *not* for bipolar disorder.

The problem of whether to extend the bipolar spectrum to children is not just theoretical. There are important clinical consequences, as shown by the dramatic increase in the prescription of antipsychotic drugs to children, including preschool children (Olfson et al., 2010). The trend has been most striking in the United States, but it has also spread to the United Kingdom (Rani et al., 2008).

Psychiatry has received criticism, both fair and unfair, for its reliance on drugs. But when we give neuroleptics to patients with schizophrenia, or mood stabilizers to patients with adult bipolar disorder, we know that the consequences of leaving the illness untreated are more severe than any side effects these agents may produce. In contrast, when we give drugs to young children who are seen as bipolar, we do not have the same evidence base and do not know the long-term consequences.

Thus, the diagnosis of bipolar disorder in children has the potential to do harm by encouraging overly aggressive pharmacological treatment. DSM-5, to its credit, tried to deal with the problem. Even so, the diagnosis of DMDD may run into the same difficulties. Child psychiatry, once noted for its interest in family life and social issues, has become focused on biological mechanisms and pharmacological solutions. These problems are made worse by seeing almost every symptom as a reflection of abnormal mood.

In summary, DSM-5, faced with demands for expanding the bipolar spectrum, acceded in some areas but held firm in others. Even so, the increase in bipolar diagnosis has already had a

profound effect on practice (Yutzy et al., 2012). Only time will tell how future generations will look back on the current practice of prescribing mood stabilizers and antipsychotics to so many patients. In 50 years, it might not be seen as a breakthrough but, rather, as a harmful fad.