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The evolution of the concept of bipolar disorder

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Kraepelin's definition of Manic Depressive Insanity, as well as his case descriptions, encompassed all recurrent major mood disorders, including what we now call bipolar disorder and «recurrent melancholia». Contemporary diagnostic systems began with DSM III in 1980 which, for the first time, attempted to establish an empirical basis for psychiatric diagnoses by developing specific descriptive criteria for each diagnosis. With respect to major affective disorders the various criteria were shown to be quite reliable, as reflected by high inter-observer coefficients in the range of 0.8.

While the establishment of this empirically based, reliable diagnostic system was a major advance for our field, a problem was created by the way the different mood disorder subgroups were organized. DSM III and IV organized the mood disorders by first identifying bipolar disorder as a separate and distinct illness «from the top», separating it from all depressive disorders. In so doing, the architects of DSM III/IV explicitly made polarity the fundamental organizing principal of all the mood disorders, with recurrence or cyclicity becoming secondary. Prior to DSM III the common understanding of Manic Depressive Illness was a recurrent endogenous mood disorder; both its endogenous and fundamentally recurrent nature distinguished it from other mood disorders that were considered «reactive» and non-recurrent.

The original distinction drawn between bipolar and unipolar (Leonhardt, Perris, Angst) was drawn from studies of patients with recurrent mood disorders, that is, patients who fit Kraepelin's description of manic depressive illness. In other words, in the studies that first defined bipolar as a distinct group, unipolar meant a form of recurrent endogenous mood disorder without mania. Similarly, when my colleagues and I first described bipolar II disorder, differentiating it from unipolar and from bipolar I, all of the patients shared the common characteristic of having a recurrent illness. It never occurred to us that «unipolar» would come to mean every depressive disorder that was not bipolar (Dunner et al., 1976).

Although DSM III/IV (fig. 1) does have a tertiary category of «recurrent depression» (under major depressive disorder) the category includes any depressed patient with more than one episode, making the category too broad to be of much use. The patients who are, in a sense, lost in the current DSM's organization are those with the more highly recurrent forms of unipolar depression, having depressive episodes with a frequency in the bipolar range, that is, with an average cycle length in the range of one to two years. By most estimates highly recurrent unipolar depression comprises 1/3rd or more of the major depression category. Although such patients are similar to their bipolar «cousins» in age of onset, frequency of recurrences, and (to a lesser extent) a bipolar family history, and some have a few symptoms analogous to mania or hypomania when depressed, as a group, highly recurrent unipolar patients are NOT bipolar. Although earlier my colleagues and I (Ghaemi et al., 2004), like Akiskal and colleagues (1983), included highly recurrent

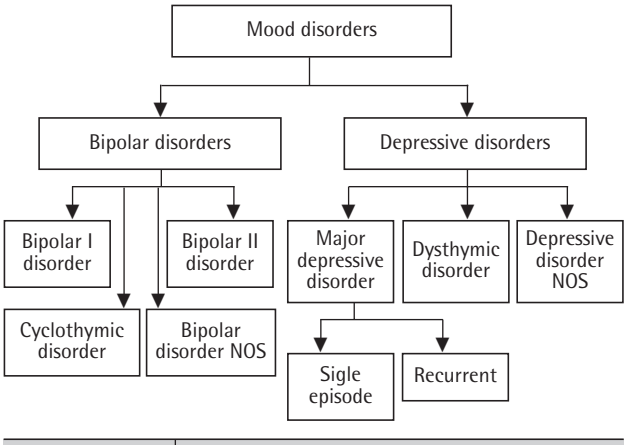

Figura 1 *DSM-IV classification of mood disorders.*

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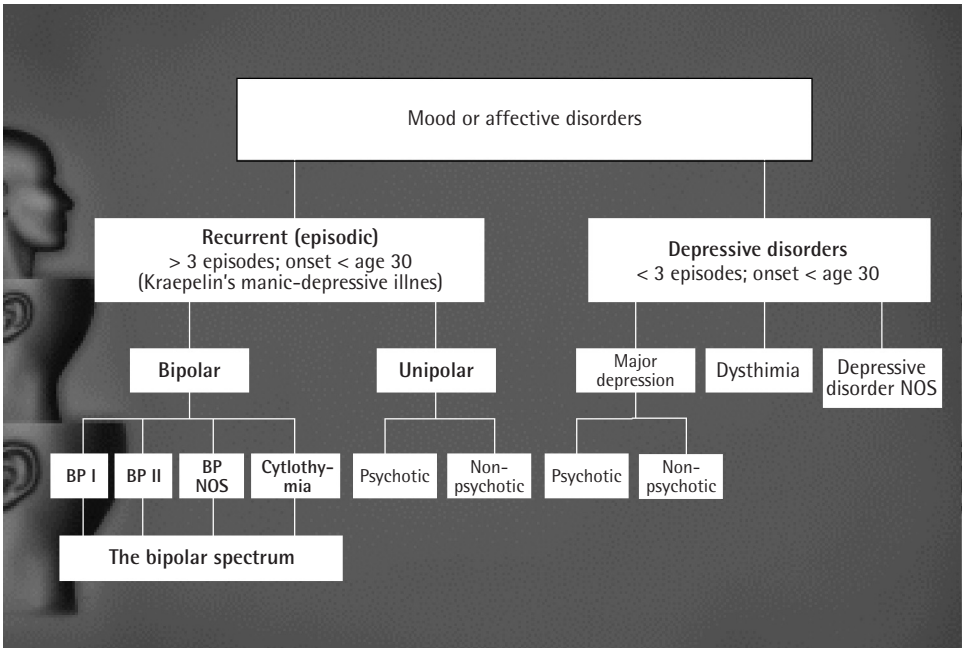

Figura 2 | *Mood or affective disorders: a proposal for DSM-V.*

unipolar depressed patients with a bipolar family history in the bipolar spectrum as a way of emphasizing their potential bipolar diathesis, I have come to feel that conceptual clarity is best maintained by acknowledging that, in terms of observable psychopathology, they are still unipolar.

The organization of the mood disorders in our current diagnostic system tends to confound polarity and cyclicity, negatively impacting clinical, genetic, and pharmacological research. Thus in clinical research on UP-BP differences, the two groups are rarely matched for cyclicity. Or in genetic linkage studies it would be of interest to know what might happen if the highly recurrent unipolar relatives of the bipolar probands were (vs. were not) included in the analysis. Finally, consider the development of new medications. Since bipolar disorder is recurrent (cyclic) almost by definition, while the broad category of unipolar depression is not, virtually all of our focus on mood stabilization focuses on the bipolar subgroup. All of our current mood stabilizers or putative mood stabilizers were developed, or are being developed, for bipolar disorder. Indeed, for all but one of them (lamotrigine) their initial therapeutic indication was for the acute treatment of mania. To my knowledge, there is not a single candidate mood stabilizer under development for the treatment of highly recurrent depression. This is spite of the fact that the most widely studied mood stabilizer for bipolar disorder, lithium, has an extensive literature (nine randomized double blind placebo controlled trials) showing that it can prevent episodes of recurrent unipolar depression every bit as effectively as it does in bipolar disorder (Davis et al.,1999; G. Goodwin and Gedddes, 2003), a finding that I would venture most American psychiatrists are not aware of.

Figure 2 represents my proposal for organizing the mood disorders in DSM V. While space does not allow a detailed discussion here, this schema does give emphasis to Kraepelin's original concept of a group of major mood disorders, characterized primarily by their tendency to recur, both with and without mania or hypomania. By making recurrence the fundamental organizing principal, the close relationship between the UP and BP patterns of recurrence would be clear. One would not have to put all recurrent UP patients in the bipolar spectrum in order to emphasize this relationship or to emphasize the importance of recurrence in many patients with UP depression.

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