Editorial

The Bipolar Spectrum

"Shrink it to Broaden it to Shrink it to Broaden it...." !

Melancholia is the beginning and a part of Mania.... The development of Mania is really a worsening of the disease (Melancholia) rather than change into another disease. (Aretaeus of Cappadocia, 100 AD).

Mania is Primary, with Depression being the consequence of preceding Mania, which means the Recurrent Unipolar subgroup of MDI does not really exist since all depressive presentations are preceded by a manic presentation. (Koukopoulos, 2006).

That Happiness and Sadness, the two normal and very common emotions of every human being, constitute the core clinical features of a disease, Manic Depressive Illness (MDI), remains a fascinating, though disturbing, fact. The magnification of joy and worry, two poles of the normal emotional spectrum, reaches such gigantic proportion necessitating treatment. The clinical presentation varying between the two poles, often alternating, naturally reveals itself as a spectrum disorder of conditions and related temperaments.

For Eugene Bleuler a patient was predominantly schizophrenic or predominantly manic-depressive in the spectrum of psychosis. But Emil Kraeplin, father of classification in modern psychiatry, segregated the two major psychotic illnesses into Manic-depressive insanity and Dementia praecox. By 1913, Kraeplin brought virtually all of the major clinical forms, which had

1. Episodic or Periodic course
2. Benign prognosis
3. Family history of MDI, under the diagnosis of Manic -Depressive illness (MDI) in which he included Bipolar Disorders (BD) and Recurrent Depressive Disorders.

The Bipolar Spectrum concept can be approached from two different ways:

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1. Manic – Depressive Spectrum: Continuum between Bipolar and Unipolar
2. Bipolar Spectrum: Restricted to BD with continuum between Full blown illness (BD I) to Milder illness to Temperament traits (Cyclothymia ……).

Understanding the concept of Bipolar/Manic Depressive Spectrum demands a brief journey into the history dating back to the last quarter of 19th century.

SHRINK IT – 1875-1925 [Figure 1]

The Northwest Wales asylum, opened in 1848, catered to a specific geographic location of the population and had admission of 3172 patients from 1875 to 1924. As depicted in the graph, mania as percentage of all admissions was 60% in 1885 which got "Shrunk" to around 20% in 1920. "In 1885, the diagnosis of mania referred to any state of OVERACTIVE INSANITY. Around 1900, primarily in response to Kraeplin's impact, the use of mania as a diagnosis in North Wales began to fall (limited only to episodic illness with benign course) progressively to about 4% in 1924.[1]"

BROADEN IT: 2nd quarter of 20th century

"Manic Depressive insanity..... includes on one hand the whole domain of periodic and circular insanity, on the other hand simple mania, the greater parts of the

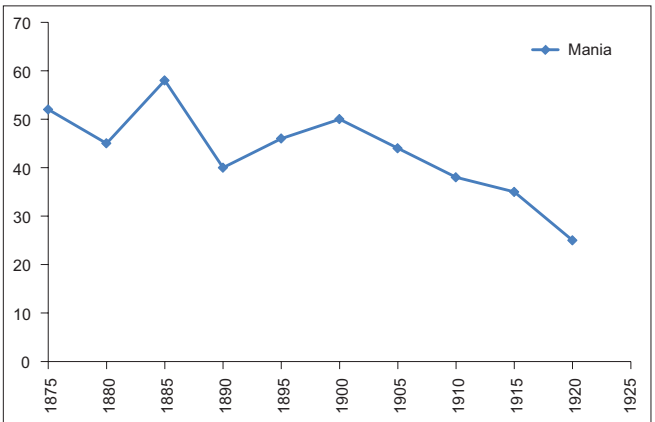
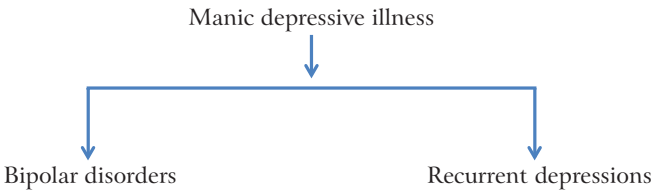


Figure 1: The diagnosis of mania as a percentage of all admissions to the north wales asylum: 1875-1924

morbid states termed Melancholia" (Emil Kreaplin, 1924).



The unifying "Broadening"concept of MDI, which brought together all the mood disorders, separating from Dementia Praecox, was based on

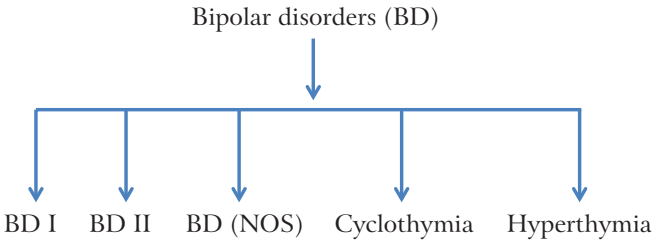
1. Episodic, recurrent course of illness
2. Benign course and outcome.

SHRINK IT (again): 2nd half of 20th Century

Move forward to the 3rd quarter and the first half of the 4th quarter of 20th century.

The Kreaplinian concept of MDI was considered "too inclusive" and in 1957 Karl Leonhard proposed the concept, propagated later by the works of Angst, 2002,[2] and Perris, of dividing the MDI into two sub groups: Bipolar and Unipolar, the only difference being presence/absence of mania. The Broad MDI concept was "shrunk again" by separating BD group away from the unipolar group. The term bipolar was introduced in DSM III in 1980 and in ICD 10 in 1992; since then the unipolar and BD are categorized as two separate diagnostic entities in the classificatory system.

"Bipolar and unipolar diseases..... have different clinical pictures. The bipolar form displays a considerably more colorful appearance; it varies not only between the two poles, but in each phase offers different pictures. The unipolar forms.... return, in aperiodic course, with the same symptomatology" (Karl Leonhard, 1979).



BROADEN IT (again): 21st Century

Since around 1990 there is an attempt to "Broaden" the concept of Bipolarity with inclusion of Soft Bipolar Disorder.

Nassir Ghaemi *et al.* Proposed separate Diagnostic Criteria for the Bipolar Spectrum Disorder:

A. At least one Major Depressive Episode
B. No Spontaneous manic or hypomanic episodes
C. Either one of the following plus at least two from D or both in C plus one in D
   1. Family history of BD in First-degree relative
   2. Antidepressant-induced mania/hypomania
D. If no items from C are present, 6 of 9 are needed:
   1. Hyperthymic personality
   2. Recurrent Major Depressive episodes (MDE) >3
   3. Brief MDEs (On average <3 months)
   4. Atypical Depressive symptoms (DSM IV Criteria)
   5. Psychotic MDE
   6. Early age of onset of MDE (<25 yrs.)
   7. Post partum depression
   8. Antidepressant "Wear off" (Acute but no prophylactic Response)
   9. Lack of response to 3 or more Antidepressant trials.

(Nassir Ghaemi, JY Ko, FK Goodwin, Jl.of Psychiatric Practice 2001;7:287-297) [Figure 2].

Source – Mood Disorders, Nassir Ghaemi, 2008 (With modifications)[3]

Do we have compelling evidence for the Bipolar Spectrum concept?

- 3-4 year follow up of 100 outpatients, by Akiskal *et al.* in 1978, diagnosed as mild depressive states variously referred to as "Neurotic", "Reactive", "Situational" etc., showed that about 20% of these patients developed mania
- Many Dysthymic children followed up, by Kovac *et al.* in 1994, beyond puberty did switch to BD without any pharmacological treatment
- Emil Kraeplin assumed Cyclothymia as part of Bipolar Spectrum
- Switch rates - Akiskal *et al.* in 1995,[4] Truman *et al.* in 2007[5] El-Mallaklh *et al.* in 2008[6] (the last two are part of STEP-BD) - in the long-term follow up

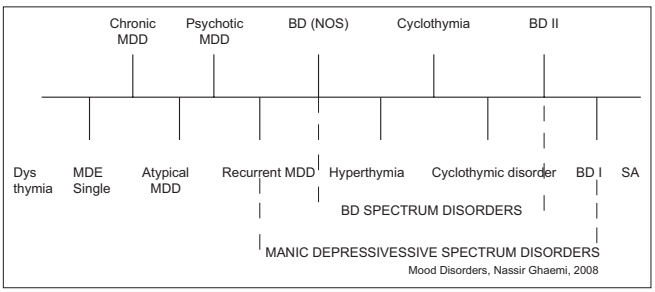


Figure 2: The affective spectrum

studies ranging from 5 to 15 years have shown that 9-40% of patients with Major Depressive Disorder (MDD) developed manic/hypomanic episodes that resulted in revisal of diagnosis to BD.

These apparently are some pointers favoring the re birth of Manic Depressive Spectrum with a significant percent of atypical, psychotic, postpartum, highly recurrent and younger age of onset depressions switching loyalty to bipolarity at a later period in the follow up.

WHY THE SPECTRUM CONCEPT?

Advantages

1. Facilitation of genetic research
2. Identification of False/Pseudo unipolars
3. Establishing the validity of Sub-Syndromal states and thereby
4. The possibility of early interventions before the onset of full-blown BD I picture
5. To increase clinicians' awareness of the close relationship between BD and MDD, which many researchers accuse of getting totally undermined in DSMIV. (DSM IV categorizes and separates BD and MDD as it separates BD and Schizophrenia)

Clinical dilemmas: In the daily practice, clinical advice is sought for a variety of behavioral problems as depicted below and the spectrum concept hopefully answers a few clinical questions in arriving at the diagnosis and plan management [Figure 3].[7]

Disadvantages

1. Theoretically and Clinically meaningless over inclusion!
2. Broadening the definition of BD to a large degree may WEAKEN the core concept of BD (Baldessarini 2000)
3. About a 100 fold increase in frequency of BD compared to 1875-1924 period!

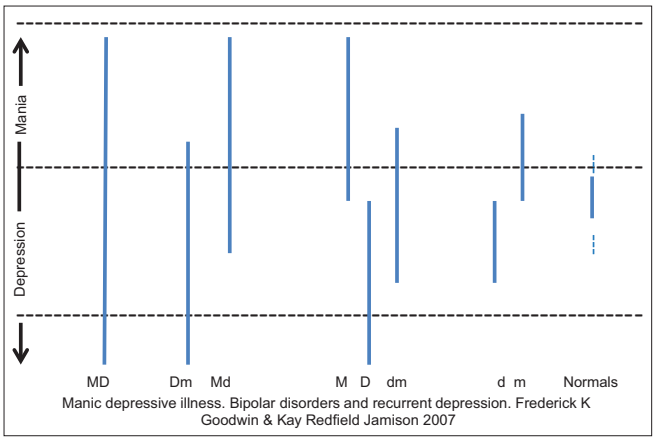


Figure 3: Range of normal mood variation by sub group

4. Damaging – Inappropriate diagnosis and treatment of persons with intense normal variants of temperament
5. As of 2008 about a million children in USA are on "Mood Stabilisers"!

Therapeutic implications

Evidence-based algorithms for treatment of Depression:

Unipolar depression: Antidepressants are the mainstay of treatment in the acute, continuation, and maintenance (Prophylaxis) phases.

Bipolar depression: Mood stabilizer is the mainstay medicine with the advice to infrequent/no use of antidepressants. Choice drugs in the acute phase are quetiapine and the combination of olanzapine and fluoxetine; in the maintenance phase lamotrigine, lithium, etc. And whenever an antidepressant is used, the dictum is that:

- It should be done at a later stage and not the first line,
- To select a drug with less switch potential (?? Less antidepressant efficacy)
- Lower dose and
- For a shorter duration possible.

Restricted/non use of antidepressants in the management of bipolar depression has been questioned by Moller *et al.* 2000[8] and remains the current hot topic of debate in psychiatry.

Therapeutic fright

Judd *et al*. 2003[9] categorically emphasized that depression is the reason for most morbidity and mortality (suicides) in BD I and BD II. The data on suicide rates in different mood disorders may vary but the widely accepted fact is that about 15% of patients with mood disorder commit suicide.

The treatment options for depression, as on today, in unipolar and bipolar are poles apart that leave eternal doubt about usage of correct and effective medication and thereby prevent suicide. "Am I on the right path in the diagnosis and treatment of this particular patient of mine suffering with depression" is the cause for the therapeutic fright!

Baldessarini[10] – "The main point…. is to encourage caution in premature and potentially misleading widening and dilution of the bipolar disorder concept. Bipolar disorder offers hope of being a coherent and tractable phenotypic target for genetic, biological, and experimental therapeutic studies. It would be tragic to weaken the core concept just as it is gaining the serious clinical and research attention that it has so long deserved."

Angst, 2007[11] –"Over decades of recurrent depressive illness, bipolar disorder may manifest at any time: a lifelong follow-up of patients hospitalised showed a persistent risk of diagnostic change to bipolar disorder of 1.25% per year of observation. An important question, then, is what proportion of patients with major depression should in fact be diagnosed as having bipolar disorder: is it one fifth or one tenth as generally reported, or as many as half, as we have found?"

The concept of spectrum disorders – Bipolar/Manic Depressive – and the subsequent dilemma in the management of depressive phase of the illness throws a kind of challenge to the practicing psychiatrist which, I am sure, was not foreseen by Emil Kraeplin and I dare not indulge in psychiatric astrology predicting the scenario in 2050.

I rest my case on this optimistic note "*Truth is the goal at which the gradual process of corrected error aims*" and humbly submit my incompetence to answer a probable question "*What does constitute the Truth*"!

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