

## ATYPICAL MIXED AND “SOFT” BIPOLAR DISORDER: DISCUSSION OF THE FREQUENTLY MISDIAGNOSED CONCEPT AND ENTITY ON FOUR CASES •

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### ATİPİK KARMA ve “SİLİK” BİPOLAR BOZUKLUK: SIKLIKLA YANLIŞ TEŞHİS EDİLEN BU KAVRAM VE ENTİTENİN DÖRT VAK'A VESİLESİYLE TARTIŞILMASI

#### ÖZET

**Amaç ve Yöntem:** “Silik bipolarite” kavramı gittikçe artan bir ilgi görmekte olup, yanlışlıkla Şizofreni, Antisosyal ve Borderline Kişilik Bozukluğu teşhisi konulan atipik duygudurumu bozukluğundan muzdarip hastaların mevcudiyeti istisna olmaktan çıkmış, kural hâlini almıştır. Bu tip hastaların tanınıp doğru teşhis ve tedaviye kavuşmaları için, bu vak'a takdiminde dört tipik “atipik” karma silik bipolar bozukluk vak'ası anlatılmıştır.

**Tartışma:** Bipolar-I Karma Durum veya Disforik Mani Depresif bir mizaçtan kaynaklanır, duygudurumuyla uyumsuz psikotik özelliklere sık rastlanır. Bipolar-II Karma Durumlar siklotimik bir mizaç üzerinde gelişen labil-irritabl duygudurumuyla karakterizedir. Bipolar-III Karma durumlarda sâdece antidepresan alırken hipomanik veya manik tablonun ortaya çıkması söz konusudur. Bipolar Bozukluk-IV Hipertimik Depresyon kategorisi ise hayat boyu süregelen hipertimik mizaca inzimam eden klinik depresyon vak'alarını kasteder. Maalesef, bu vak'aların hiç biri mevcut nozolojilerde tanımlanmamıştır. Bizim sunduğumuz dört vak'a ise bu kategorilerin tipik örneklerini oluşturmaktadır. Aslında, bütün psikiyatrik sendromlar için, mevcut taksonomilerdeki indirgeyici “kutupsal” yaklaşımın, “süreklilik” yaklaşımının ışığı altında, yeniden sorgulanması gerekmektedir.

**Bulgular:** Doğru teşhis ve tedaviyle dört vak'ada da olumlu sonuçlar alınmıştır.

**Sonuç:** Gerek tedavi gerekse prognoz açılarından sahip oldukları çarpıcı farklılıklar ve yüksek morbidite ile süsüdalite ve düşük hayat kalitesi göz önüne alındığında, bu vak'aların doğru olarak tanınmaları ve tedavi edilmelerinin önemi daha da belirginleşmektedir.

**Anahtar Kelimeler:** atipik karma bipolar durumlar, silik bipolarite, hipertimik mizaç, siklotimi, duygudurumu bozuklukları

#### ABSTRACT

**Objective and Method:** The concept of “soft bipolarity” is gaining an increasing interest and the existence of atypical mixed mood disordered patients is not an exception anymore but it is rather a rule. In this case presentation, four typical “atypical” cases of mixed soft bipolar disorder are described.

**Discussion:** Bipolar-I Disorder Mixed State or Dysphoric Mania arises from a depressive temperament. Mood incongruent psychotic features can often be observed. Bipolar-II Disorder Mixed States or mixed states with labile-irritable mood arise from a cyclothymic temperament. Bipolar-III Disorder Mixed State patients generally progress into hypomanic and manic episodes while on antidepressant therapy. Bipolar Disorder-IV Hyperthymic Depression category includes those having clinical depression that is superimposed on lifelong hyperthymic temperament. Unfortunately, neither of these mixed states are a part of current official nosologies. These four cases are typical examples of these categories. As a matter of fact, the present reductionist concept of “polarity” should be reconsidered and argued with the aid of the “continuum” concept.

**Results:** With the proper diagnosis and treatment, all of the cases improved to a significant degree.

**Conclusion:** Regarding the strikingly favorable differences both in therapeutic and prognostic aspects, it is

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mandatory to recognize and treat these cases correctly because of the high rates of morbidity, suicidal mortality and low quality of life.

**Keywords:** atypical mixed bipolar states, soft bipolarity, hyperthymic temperament, cyclothymia, mood disorders

## PURPOSE

Current nosology describes “depressive mania” as a mixture of full syndromal mania and full syndromal depression. Though there is no official terminology describing mixed states other than mixed or dysphoric mania, experience indicates that many different clinical variants exist within this spectrum. Bipolar Disorder has been traditionally considered to have 1% prevalence in general population but there is epidemiological data indicating that at least 5% of the general population is included in the bipolar spectrum (Angst 1998).

Almost a hundred years ago, Kraepelin described “mood”, “thought” and “psychomotor activity” features that are inconsistent with each other. If all were increased the disorder was “classical mania”; if all were decreased “classical retarded depression” took place. If one of the domains were contrary to the others (for instance depressed mood, flight of ideas and increased motor activity), then “depressive mania” would be diagnosed. Anxious mood along with anxious mania, irritable mood along with irascible mania, depressive mood with retardation in thought and increased motor activity along with agitated depression, depressed mood with psychomotor retardation and flight of ideas along with depression with flight of ideas were among those that were described. He concluded that these were all manifestations of a single morbid process linked by common temperamental and familial genetic factors (Goodwin 1990)

Although “depression with flight of ideas” and “agitated depression” are often seen in clinical practice, they have been ignored by DSM-IV (American Psychiatric Association 1994) and ICD-10 (World Health Organisation 1992) and it is an obligation to revise and modify the criteria describing mixed states. The clinical importance of brief recurrent depressions and minor depressive disorders are also a point of controversy (Altamura et al. 1995). The need of a new conceptualization of “temperament” is also stressed (Perugi et al. 1998, Akiskal 1999).

When bipolarity and temperament are evaluated, mixed states drawing our attention are:

Bipolar-I Disorder Mixed State or Dysphoric Mania arises from a depressive temperament, mood incongruent psychotic features can often be observed. Alcohol abuse is very common. These patients are usually misdiagnosed as schizophrenia. In these circumstances, positive family history for bipolarity points out to a bipolar nature.

Bipolar-II Disorder Mixed States or mixed states with labile-irritable mood arise from a cyclothymic temperament. These patients are misdiagnosed as “borderline personality disorder” because of their “stable unstable” life courses. Although according to DSM-IV, a hypomanic period of 4 days or more is required in order to diagnose BD-II, recent studies point out to a modal distribution of hypomania lasting from 1 to 3 days (Akiskal 1996b). When Major Depressive Disorder (MDD) is superimposed on this basic structure, the instability that occurs in this cyclothymic person’s life causes him to be stigmatized with an Axis-II diagnosis. Caffeine and stimulant usage or abuse is very common among these patients. Mood lability, which is characteristic among these patients, is not required for the diagnosis of hypomanic states that are described in DSM-IV. In contrast, this mood lability is a strong determinant of an impending hypomanic period in MDD patients (Akiskal et al. 1995). In this cyclothymic patient population, many of the members present with depressive mood swings rather than showing full-blown hypomanic features. This moodiness makes it easier for the faulty diagnosis of Borderline Personality Disorder if DSM-IV criteria are strictly applied.

Bipolar-III Disorder Mixed State patients generally progress into hypomanic and manic episodes while on antidepressant therapy. These episodes seem different from the ones that are experienced only during antidepressant therapy. According to clinical observations, many of these patients are diagnosed as Early Onset Dysthymia according to DSM-IV terminology. What differentiates them from common dysthymic individuals is that, they usually have a po-

sitive family history of Bipolar Disorder. Stimulant masked or unmasked states can be seen in Bipolar Disorder-III cases. These states are actually similar to the episodes seen during antidepressant therapy. This category should include those who will otherwise be misdiagnosed as having Substance Related Mood Disorders.

Bipolar Disorder-IV Hyperthymic Depression category includes those having clinical depression that is superimposed on life-long hyperthymic temperament. These patients are usually misdiagnosed as sociopaths (Antisocial Personality Disordered patients) but they are typically generous to their sexual partners. In contrast to Bipolar-I and Bipolar-II's hypomanic periods, their hyperthymic states are life-long. When a hyperthymic person develops depression, the onset is usually hypersomnic and retarded. Their depressions possess hyperthymic features like increased sexuality and flight of ideas. Antidepressants tend to destabilize these traits (Akiskal and Mallya 1987).

Unfortunately, neither of these mixed states are a part of current official nosology and even the disease concepts differ in-between USA and Europe (Cooper et al. 1972).

The purpose of this case presentation is to inform the colleagues about typical "atypical" cases that we treated with a high rate of remission.

## CASE REPORTS

1. A 34 years old woman with a long standing chaotic, erethistic, erratic and erotic life style was referred for her MDD episode. She was a heavy smoker and alcohol abuser. She had committed suicide for three times by taking drugs. Two separate psychiatrists saw her on several occasions and she was diagnosed as "Double Depression with Borderline Personality Disorder". After three months' treatment with fluoxetine 20 mgs per day, her symptoms improved moderately but she was still unhappy, having more inappropriate casual affairs and becoming depressed and even suicidal after them. Following careful re-evaluation, we changed the diagnosis to "Bipolar-III Mixed State", quitted fluoxetine and started giving valproate 1000 mg/day. Since the last two years she is happy, stable, working hard in her job and preparing to marry a new boy friend.

2. A talented academician in his early forties was

examined for his moodiness and recurrent depressive states and frequent migraine headaches. His generous hospitality and high success in academic field was striking. On the other hand, his wife was tired and bored of his anger outbursts and moodiness. He used to shout at and even beat his 6 years old son for minor things. He frequently experienced serious depressive episodes lasting no more than one to three days, followed by his usual hyperthymic state. He was misdiagnosed as a "clever sociopath" by a former psychiatrist. He was very generous to his wife in his "good times". His hyperthymic state was life-long with a strong family history of "all the male, even female members of the family behaving like him". When he develops depression, the onset is usually hypersomnic and retarded. Even during these depressive periods he possesses hyperthymic features like increased sexuality and flight of ideas. Imipramine as monotherapy destabilized these traits and lithium was added with a mild control of his behavioral problems and migraine attacks. After reevaluation, his medication was switched to valproate and imipramine 25 mgs per day. All his behavioral problems, mood disorder and migraine attacks reduced to a significant degree in weeks' duration and he was quite healthy during the following 12 months. He is a typical Bipolar-IV Hyperthymic Depression(s) case.

3. A 28 years old single woman, a real doctor shopper, was examined for her multiple physically unexplainable bodily complaints, subpanic and panic attacks, moodiness, demanding and erratic temperament. She was previously diagnosed as having "Somatization Disorder with Histrionic Personality Disorder". According to her statement paroxetine 40 mgs per day combined with trifluoperazine 2 mgs per day empirically reduced her complaints "50%" only but she managed to marry. An insight-oriented cognitive approach from an experienced psychotherapist for four months only created negative counter-transference! Some days she would telephone three to four times just for "nothing". Whenever a dose regulation or a change in the treatment planning was offered, she would resist with a cynical smile on her face resembling the famous so called "la belle indifference" and we had to spend a lot of time for persuasion. The same negative counter-transference developed in all of us and we made an offer to her to see some other colleague. This "marvelous idea" was

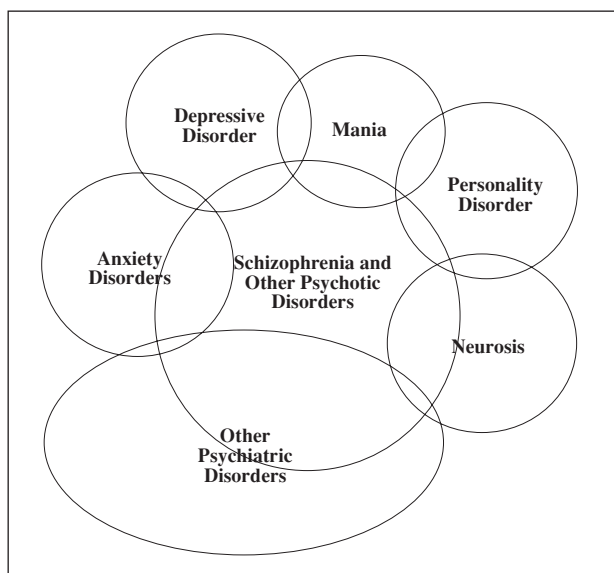
surprisingly rejected by her, raising the question about an additional diagnosis of “Self-Defeating Personality Disorder”. In the classical sense, she was a terrible neurotic! During an overview session between colleagues, we suddenly discovered the “chance” of soft bipolarity for her (and, to be honest, for us)! After an hour’s “battle” with and a week’s hesitation by her, she began taking valproate. The initiation of this treatment has been about nine months. She is taking valproate 500 mgs and paroxetine 5 mgs per day. The Somatization and all the Personality Disorders she possessed are “miraculously” cured. Everybody is happy after all; including the patient, her husband and us! The diagnosis was somewhere in-between Bipolar-II or Bipolar-III Mixed State.

4. A 34 years old single woman with a high educational career was referred for her problematic alcohol and caffeine abuse, excessive smoking and depressive complaints. She is the daughter of a sophisticated and a well-known family. His father, a famous lawyer, had near-end stage carcinoma. During evaluation, she confessed that she would drink a big bottle of whisky and 150 mgs of diazepam together on some occasions. When she was younger, she had a “high” life with a lot of affairs, one-night stands and “dancing and drinking for hours without getting tired and going to school next morning with almost no sleepiness”. She used to become “down” time by time and was treated with psychoanalysis for four ye-

ars, which she “enjoyed very much” and abandoned after “getting bored with it”. Another psychiatrist gave her an SSRI, diazepam “instead of alcohol” and “suggestions about life” with the only “benefit” of cross-dependence between alcohol and diazepam. She was seriously depressed after the initial diagnosis of her father’s disease and lost a lot of weight. During the interview, her affect and mood were depressed with remarkable irritability and her associations were slightly accelerated leading to circumstantialities though she was not obsessive at all. After psycho-education about the concept of soft bipolarity, she accepted to take mirtazapine 45 mgs and valproate 500 mgs per day. It has been 6 months since the treatment was initiated. During this period her father passed away; a lot of problems occurred; but she managed to overcome them without any deterioration. She reduced her “self-medication with alcohol” to the degree of casual drinking of two to four glasses only. She is also a case somewhere in-between Bipolar-II or Bipolar-III Mixed State.

## DISCUSSION

Although their existence is not an exception but rather a rule; these “soft bipolar” cases are either misdiagnosed, underdiagnosed or classified under the “Not Otherwise Specified” trash-box of DSM-IV and both their evaluation and treatment-management approaches are quite distinct than the Bipolar-I and Bipolar-II cases (Aksaray et al. 2000). Manic switch is a well-documented problem in the treatment of patients who receive antidepressants for any purpose (Stoll et al. 1994) and from any pharmacological group (Howland 1996). Although still highly controversial, switch to rapid-cycling (i.e. 4 or more episodes in one year) is a matter of attention (Altshuler et al. 1995). Some research indicate that antidepressants induce mania and/or rapid cycling (Wehr et al. 1988, Coryell et al. 1992, Hurowitz and Liebowitz 1993). Others approach to the idea with great skepticism, claiming that manic episode appears because the patient was an already undiagnosed bipolar (Wehr 1993). Although the current taxonomies like DSM-IV and ICD-10 prefer the reductionist “polarity” concept founded by the Newcastle school from England, the “continuum” concept is a well-known argument since Aubrey Lewis (1938), stating that mood disorders constitute a continuum of anxiety disorders, from



**Figure 1**

mild neurotic depressions, severe endogenous depressions to psychotic depression. Indeed, recent data suggests that probably the continuum concept is more close to the truth (Akiskal 1996a, Perugi et al. 1998). This is in harmony with the concept that mental disorders are not distinct entities; rather, they merely reflect the prominent or dominant clinical presentations, though the patho-physiological mechanisms might be quite close. This is true even for distinct entities like schizophrenia when the clinical and biological facts are reviewed and diagnostic stability of patients who were diagnosed once as having Schizophrenia, Schizoaffective Disorder or Bipolar Disorder vary greatly during the longitudinal follow-up (Cooper et al. 1972, Berrettini 2000, Kuruoğlu et al. 2001). This approach is reasonable for the common sense which questions the validity and specificity of ill-defined entities like Schizoaffective Disorder, Mood Disorder With Mood-Incongruent Psychotic Symptoms and all of the “trash-box” category of NOSs (Not Otherwise Specified). According to our conceptualization, the “continuum concept” for all neuropsychiatric conditions can be schematized in Figure 1.

## CONCLUSION

The underlying biological, patho-physiological and biological mechanisms can also be quite different or modified in typical bipolars and soft (Akiskal and Mallya 1987, Akiskal 1994, Akiskal 1996a) or atypical mixed (Dell’Osso et al. 1991, Akiskal et al. 1995) or brief, subsyndromal (Judd et al. 1997) and recurrent mood states (Baldwin and Sinclair 1997). This is an important point of view especially when the relative ineffectiveness of lithium and generally beneficial effects of anticonvulsants like valproate, carbamazepine, gabapentin, lamotrigine and atypical or new generation antipsychotics like clozapine, olanzapine (Manji et al. 2000). All MDD, anxiety disorder and even Cluster B personality disorder (especially the Borderline and Antisocial) cases should be carefully evaluated in terms of the differential diagnosis of soft or atypical mixed bipolarity.

## KAYNAKLAR

- Akiskal HS, Mallya G. Criteria for the “soft” bipolar spectrum: treatment implications. *Psychopharmacol Bulletin* 1987; 23:68-73.
- Akiskal HS. Temperaments on the border of affective disorders. *Acta Psychiatr Scand* 1994; 89[suppl 379]:32-37.
- Akiskal HS, Maser JD, Zeller P, et al. Switching from “unipolar” to “bipolar”: an 11-year prospective study of clinical and temperamental predictors in 559 patients. *Arch Gen Psychiatry* 1995; 52:114-123.
- Akiskal HS. The prevalent clinical spectrum of bipolar disorders: beyond DSM-IV. *J Clin Psychopharmacol* 1996a; 16[suppl 1]:4S-14S.
- Akiskal HS. The prevalent clinical spectrum of bipolar disorder. *Clin Psychopharmacol* 1996b; 17(suppl3):117-122.
- Akiskal HS. Depression: The Complexity of its Interface with Soft Bipolarity. In: *Depressive Disorders*, Maj M, Sartorius N, eds. WPA Series Evidence and Experience in Psychiatry, Vol1, John Wiley & Sons, England, 1999, p. 68-71.
- Aksaray G, Yenilmez \*, Kortan G, Kaptanoğlu C. Mixed mania: clinical characteristics and treatment. *Psychiatry in Türkiye* 2000; (1):1-9.
- Altamura AC, Carta MG, Carpinello B, et al. Lifetime prevalence of brief recurrent depression (results from a community survey). *Europ Neuropsychopharmacol* 1995; 5(suppl):99-102.
- Altshuler LL, Post RM, Leverich GS, Mikalaukas K, Rosoff A, Ackerman L. Antidepressant-induced mania and cycle acceleration : a controversy revisited. *Am J Psychiatry* 1995; 152:1130-1138.
- American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders - Fourth Edition, DSM-IV*. American Psychiatric Association, Washington, DC, 1994.
- Angst J. The emerging epidemiology of hypomania and bipolar disorders. *J Affect Dis* 1998; 50:143-151.
- Baldwin DS, Sinclair JMA. Recurrent Brief Depression: ‘Nasty, Brutish and short’ In *Troublesome Disguises - Underdiagnosed Psychiatric Syndromes*, Bhugra D, Munro A, eds. Blackwell Science, Oxford, 1997, p. 226-240.
- Berrettini WH. Are schizophrenic and bipolar disorders related? A review of family and molecular studies. *Biol Psychiatry* 2000 Sep 15; 48(6):531-538.
- Cooper JE, Kendell RE, Garland BJ, et al. *Psychiatric Diagnosis in New York and London*. Oxford University Press, London, 1972.
- Coryell W, Endicott J, Keller M. Rapid cycling affective disorder: demographics, diagnosis, family history, and course. *Arch Gen Psychiatry* 1992; 49:126-131.
- Dell’Osso L, Nassi R, Akiskal HS, et al. The manic-depressive mixed state: familial, temperamental and psychopathologic characteristics in 108 female inpatients. *Eur Arch Psychiatry Clin Neurosci* 1991; 240:234-239.
- Goodwin FK, Jamison KR. *Manic-Depressive Illness*. Oxford University Press, New York, 1990.
- Howland RH. Induction of mania with serotonin reuptake inhibitors. *J Clin Psychopharmacol* 1996; 16:245-427.
- Huowitz GI, Liebowitz MR. Antidepressant-induced rapid

- cycling: six case reports. *J Clin Psychopharmacol* 1993; 13:52-56.
- Judd LL, Akiskal HS, Paulus MP. The role and clinical significance of subsyndromal depressive symptoms (SSD) in unipolar major depressive disorder. *J Affect Disord*, 45(1-2):5-17, 1997; discussion 17-18.
- Kuruoğlu A, Önder F, Arıkan Z, Işık E. Diagnostic stability in chronic schizophrenia, schizoaffective disorder and bipolar affective disorder (translate). *Yeni Symposium* 2001; 39:8-12.
- Lewis A. States of depression: their clinical and aetiological differentiation. *Br Med J* 1938; 2:875.
- Manji HK, Bowden CL, Belmaker RH editors. *Bipolar Medications - Mechanism of Action*. American Psychiatric Press, 2000.
- Perugi G, Akiskal HS, Lattanzi L, Cecconi D, Mastrocinque C, Patronelli A, Vignoli S. The high prevalence of soft bipolar (II) features in atypical depression. *Comp Psychiatry* 1998; 39:63-71.
- Stoll AL, Mayer PV, Kolbrener M. Antidepressant-associated mania: a controlled comparison with spontaneous mania. *Am J Psychiatry* 1994; 151:1642-1645.
- Wehr TA, Sack DA, Rosenthal NE, Cowdry RW. Rapid cycling affective disorder: contributing factors and treatment response in 51 patients. *Am J Psychiatry* 1988; 145:179-184.
- Wehr TA. Can antidepressants induce rapid cycling? *Arch Gen Psychiatry* 1993; 50:495-496.
- World Health Organisation. *The ICD-10 Classification of Mental and Behavioural Disorders: Clinical Descriptions and Diagnostic Guidelines*. World Health Organisation, Geneva, 1992.