BIPOLAR DISORDER

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Bipolar Disorder: What is it?

- Bipolar disorder (manic-depressive illness) is referred as an episodic and lifelong and clinically severe mood disorder
- Mania/ manic episode: an elevated, euphoric, and expansive mood, often interfered by outbursts of strong irritability or violence—particularly when others do not go with the manic person's wishes and thoughts
- Depressive episode: markedly depressed mood or loss of interest in pleasurable activities

General Features

- Manic and hypomanic periods are tend to be shorter than depressive periods
- Hard to distinguish from unipolar major depression
- Tends to have psychotic features too
- Impairment of occupational and social functioning,
 - hospitalization might be necessary in manic episodes

Bipolar Disorder: Types

Cyclothymic Disorder

Bipolar I

Bipolar II

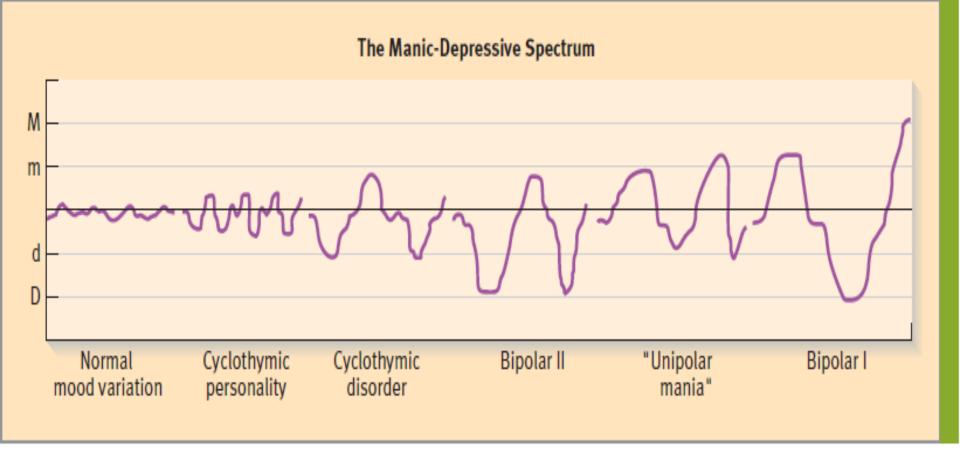


FIGURE 7.7

The Manic-Depressive Spectrum

There is a spectrum of bipolarity in moods. All of us have our ups and downs, which are indicated here as normal mood variation. People with a cyclothymic personality have more marked and regular mood swings, and people with cyclothymic disorder go through periods when they meet the criteria for dysthymia (except for the 2-year duration) and other periods when they meet the criteria for hypomania. People with bipolar II disorder have periods of major depression and periods of hypomania. Unipolar mania is an extremely rare condition. Finally, people with bipolar I disorder have periods of major depression and periods of mania. (Adapted from Goodwin & Jamison, 2009.)

Source: From Frederick K. Goodwin and Kay R. Jamison. (2009). Manic depressive illness. Copyright © 1990 Oxford University Press, Inc. Used by permission of Oxford University Press, Inc.

DSM-IV-TR

Criteria for Cyclothymic Disorder

- A. For at least 2 years, the presence of numerous periods with hypomanic symptoms and numerous periods with depressive symptoms that do not meet criteria for a Major Depressive Episode. Note: In children and adolescents, the duration must be at least 1 year.
- B. During the above 2-year period (1 year in children and adolescents), the person has not been without the symptoms in Criterion A for more than 2 months at a time.
- C. No Major Depressive Episode, Manic Episode, or Mixed Episode has been present during the first 2 years of the disturbance. Note: After the initial 2 years (1 year in children and adolescents) of Cyclothymic Disorder, there may be superimposed Manic or Mixed Episodes (in which case both Bipolar I Disorder and Cyclothymic Disorder may be diagnosed) or Major Depressive Episodes (in which case both Bipolar II Disorder and Cyclothymic Disorder may be diagnosed).
- D. The symptoms in Criterion A are not better accounted for by Schizoaffective Disorder and are not superimposed on Schizophrenia, Schizophreniform Disorder, Delusional Disorder, or Psychotic Disorder Not Otherwise Specified.
- E. The symptoms are not due to the direct physiological effects of a substance (e.g., a drug of abuse, a medication) or a general medical condition (e.g., hyperthyroidism).
- F. The symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.

Cyclothymic
Disorder: persists for at least 2 years, lacks certain extreme symptoms and psychotic features

Source: Reprinted with permission from the American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition,

case study A Cyclothymic Car Salesman

A 29-year-old car salesman was referred by his current girlfriend, a psychiatric nurse, who suspected he had a mood disorder even though the patient was reluctant to admit that he might be a "moody" person. According to him, since the age of 14 he has experienced repeated alternating cycles that he terms "good times and bad times." During a "bad" period, usually lasting 4 to 7 days, he sleeps 10 to 14 hours daily [and] lacks energy, confidence, and motivation—"just vegetating," as he puts it. Often he abruptly shifts, characteristically upon waking up in the morning, to a 3- to 4-day stretch of overconfidence, heightened social awareness, promiscuity, and sharpened thinking—"things would flash in my mind." At such times he indulges in alcohol to enhance the experience, but also to help him sleep. Occasionally the "good" periods last 7 to 10 days but culminate in irritable and hostile outbursts, which often herald the transition back to another period of "bad" days. . . .

In school, A's and B's alternated with C's and D's, with the result that the patient was considered a bright student whose performance was mediocre overall because of "unstable motivation." As a car salesman his performance has also been uneven, with "good days" canceling out the "bad days"; yet even during his "good days" he is sometimes perilously argumentative with customers and loses sales that appeared sure. Although considered a charming man in many social circles, he alienates friends when he is hostile and irritable. . . . (Spitzer et al., 2002, pp. 155–56)

- Bipolar I: at least one manic episode or mixed episode
- **Bipolar II:** the person does not experience full-blown manic (or mixed) episodes

Experience of clear-cut hypomanic episodes as well as major depressive episodes as in bipolar I disorder

DSM-IV-TR

Criteria for Bipolar I and Bipolar II Disorder

Bipolar I Disorder

There are six separate criteria sets for Bipolar I Disorder: Single Manic Episode, Most Recent Episode Hypomanic, Most Recent Episode Manic, Most Recent Episode Mixed, Most Recent Episode Depressed, and Most Recent Episode Unspecified.

Bipolar I Disorder, Single Manic Episode, is used to describe individuals who are having a first episode of mania. The remaining criteria sets are used to specify the nature of the current (or most recent) episode in individuals who have had recurrent mood episodes.

Bipolar II Disorder (Recurrent Major Depressive Episodes with Hypomanic Episodes)

- A. Presence (or history) of one or more Major Depressive Episodes.
- B. Presence (or history) of at least one Hypomanic Episode.
- C. There has never been a Manic Episode or a Mixed Episode.
- D. The mood symptoms in Criteria A and B are not better accounted for by Schizoaffective Disorder and are not superimposed on Schizophrenia, Schizophreniform Disorder, Delusional Disorder, or Psychotic Disorder Not Otherwise Specified.
- The symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.

Source: Reprinted with permission from the American Psychiatric Association.

Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition,

Text Revision (Convright © 2000). American Psychiatric Association.

case study Roller Coaster

When Ernest Eaton's desperate wife finally got him to agree to a comprehensive inpatient evaluation, he was 37, unemployed, and had been essentially nonfunctional for several years. After a week during which he was partying all night and shopping all day, Mrs. Eaton said she would leave him if he did not check into a psychiatric hospital. The admitting psychiatrist found him to be a fast-talking, jovial, seductive man with no evidence of delusions or hallucinations.

Mr. Eaton's troubles began 7 years before when he . . . had a few months of mild, intermittent depressive symptoms, anxiety, fatique, insomnia, and loss of appetite, [but] within a few months he was back to his usual self. A few years later . . . after removal of [an asymptomatic] mass . . . Mr. Eaton noted dramatic mood changes. Twenty-five days of remarkable energy, hyperactivity, and euphoria were followed by 5 days of depression during which he slept a lot and felt that he could hardly move. This pattern of alternating periods of elation and depression, apparently with few "normal" days, repeated itself continuously over the following years.

During his energetic periods, Mr. Eaton was optimistic and selfconfident but short tempered and easily irritated. His judgment at work was erratic. He spent large sums of money on unnecessary and, for him, uncharacteristic purchases, such as a high-priced stereo system and several Doberman pinschers. He also had several impulsive sexual flings. During his depressed periods, he often stayed in bed all day because of fatigue, lack of motivation, and depressed mood. He felt guilty about the irresponsibilities and excesses of the previous several weeks. He stopped eating, bathing, and shaving. After several days of this withdrawal, Mr. Eaton would rise from bed one morning feeling better and, within 2 days, he would be back at work, often working feverishly, though ineffectively, to catch up on work he had let slide during his depressed periods. (Adapted with permission from DSM-IV-TR Casebook: A Learning Companion to the Diagnostic and Statistical Manual of Mental Disorders. Fourth Edition. Text Revi-

Panel 1: DSM-IV classification of bipolar disorders

DSM-IV category Bipolar I disorder	Criteria One or more manic or mixed episodes, usually accompanied by one or more major depressive episodes	Course specifiers and examples To describe current (or most recent) episode: Mild, moderate, severe without psychotic features Severe with psychotic features In partial or full remission With catatonic features With postpartum onset		
		To describe current (or most recent) major depressive episode: Chronic With melancholic features With atypical features		
		To describe pattern of episodes: With or without full interepisode recovery With seasonal pattern With rapid cycling (≥4 episodes in previous 12 months)		
Bipolar II disorder	Recurrent major depressive episodes with one or more hypomanic (milder than manic) episodes	To describe current (or most recent) episode: Hypomanic Depressed		
		To describe current (or most recent) major depressive episode and pattern of epsiodes: See bipolar I disorder		
Cyclothymic disorder	Chronic (>2 years), fluctuating mood disturbance, involving numerous periods of mild hypomanic and depressive symptoms that do not meet criteria for a major depressive episode	Over 2 years any symptom-free intervals last no longer than 2 months		
Bipolar disorder not otherwise specified	Disorders with bipolar features that do not meet criteria for any specific bipolar disorder	Examples: Very rapid cycling (over days) Recurrent hypomanias without depressive symptoms Indeterminate whether primary or secondary (due to a general medical condition or substance abuse)		
DSM-IV=Diagnostic and	Statistical Manual of Mental Disorders, 4th edn.			

Bipolar Disorder in History

- Has its roots in the work of the Greek physicians of the classical period
- Mania and melancholia are two of the earliest described human diseases
- Classical Era and Hippocrates: mania, melancholia, paranoia, deliria, hysteria
- Aretaeus: eclecticism, biological causes and melancholia

In the classical era four meanings of 'mania' were described:

- A reaction to an event with the meaning of rage, anger or excitation (like Homer in his Iliad who described 'Aias maenomenos', meaning 'Ajax in a rage')
- A biologically defined disease (Hippocrates, Aretaeus of Cappadocia and others)
- 3. A divine state (Socrates, Plato)
- A kind of temperament, especially in its mild form (Hippocrates)

The position of Aretaeus, as described in his two books, can be summarized as following (Marneros, 1999):

- Melancholia and mania have the same aetiology, namely disturbances of the function of the brain and some other organs.
- Mania is a worsening of melancholia.
 Mania is the phenomenological counterpart of
- melancholia.

 4. His concepts of melancholia and mania were broader than the modern concepts: depression,
- broader than the modern concepts: depression, psychotic depression, schizoaffective disorders, mixed states, schizophrenia with affective symptomatology and some organic psychoses were involved.
- He differentiated between melancholia, which is a biologically caused disease, and reactive depression, a psychologically caused state.

- Jean-Pierre Falret: "a circle of both types one single disease."
- The modern concept: in France, 19th century, hospital La Salpetriere, Jean-Pierre Falret.
- Emil Kraepelin "the father of 3 modern psychiatry"
- Counter arguments to bipolar disorder
- Re-birth of bipolar disorder: Jules Angst 1966, Switzerland

- Genetic and environmental factors have a synergic impact on the aetiology of endogenous depression.
- Gender plays an important role in the aetiology of endogenous depression. There is a relationship between female gender and endogenous depression, but bipolar disorders are equally represented in males and females.
 - Manic-depressive illness is nosologically not homogeneous. Unipolar depression differs significantly from bipolar disorders in many characteristics such as genetics, gender, course and premorbid personality.
- Late-onset depression (Kraepelin's 'Involutionsmelancholie') seems to belong to unipolar depression and has only a weak relationship to bipolar disorders.

Epidemiology

- Bipolar disorder is seen equally in both men and women but the depressive episodes are more common in women
- Average age of onset is 18-22
- Bipolar II occurs around 5 years later than Bipolar I
- Both recurrent

United States

The life time prevalence of Bipolar I: around 0.6%

The life time prevalence of Bipolar II: around 0.8%

(Merikangas, 2007)

Table 1. Lifetime and 12-Month Prevalence and Age at Onset of DSM-IV/CIDI Bipolar Disorder in the 9282 Respondents

	Any BPD	BP-I	BP-II	Subthreshold BPD
Prevalence, mean (SD)				
Lifetime	4.4 (24.3)	1.0 (13.2)	1.1 (10.6)	2.4 (23.3)
12 mo	2.8 (18.9)	0.6 (9.2)	0.8 (9.9)	1.4 (15.1)
Age at onset, y*	` ′	` '	` '	` ′
Mean (SE)	20.8 (11.8)	18.2 (11.6)	20.3 (9.7)	22.2 (12.6)
IQR† `	12.6-24.9	12.3-21.2	12.1-24.0	13.0-28.3

Abbreviations: BPD, bipolar disorder; BP-I, DSM-IV bipolar I disorder; BP-II, DSM-IV bipolar II disorder; CIDI, Composite International Diagnostic Interview; IQR, interguartile range.

†The range between the 25th and 75th percentiles on the age-at-onset distribution.

^{*}Retrospectively reported age at onset of the first manic/hypomanic or major depressive episode. The means differ significantly across the 3 BPD subgroups at the P=.05 level using a 2-sided test (χ_2^2 =7.8; P=.02).

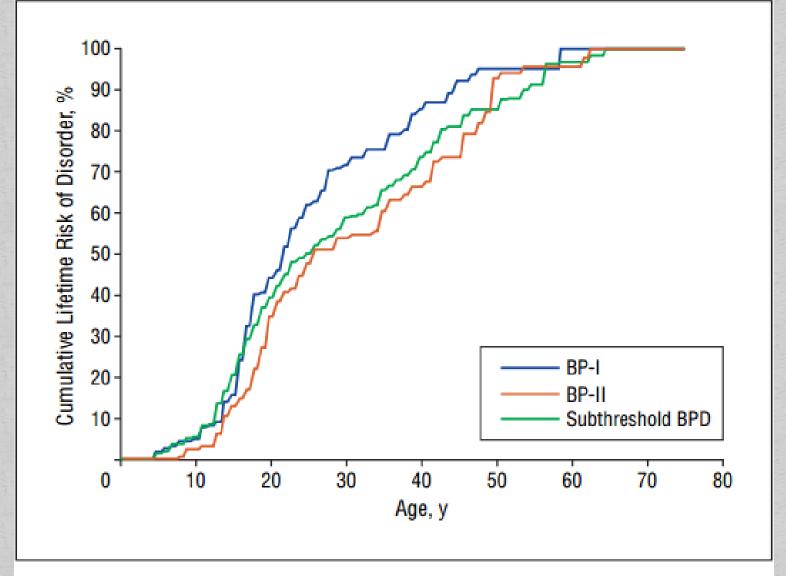


Figure. Cumulative age-at-onset distributions of the DSM-IV/Composite International Diagnostic Interview bipolar disorders (BPDs) in respondents projected to develop these disorders in their lifetime. Onset is defined as the age at the first occurrence of either a manic/hypomanic or a major depressive episode.

Europe

The life time and 12 months prevalence of Bipolar disorder in general: around 0.9%

Bipolar II > Bipolar I

(Pini, Stefano, 2005)

Cross-Cultural Prevalence of Depression Rates

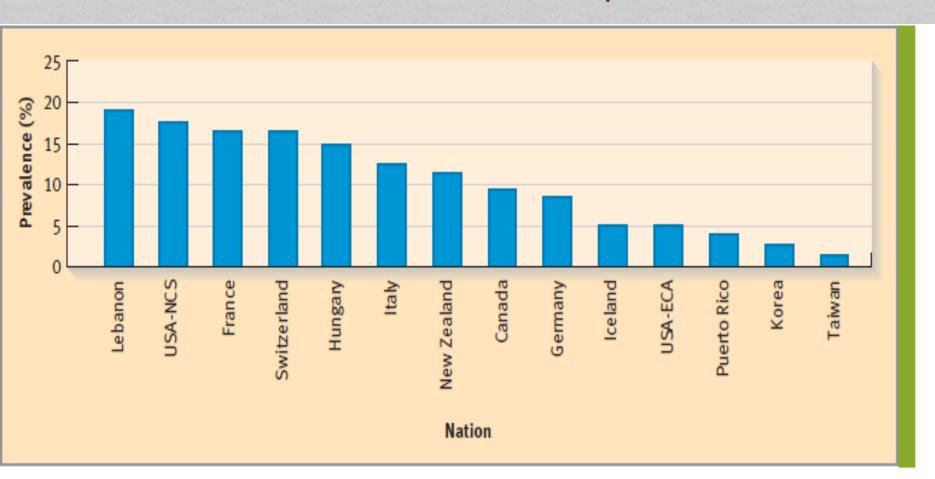


FIGURE 7.8

Prevalence Rates for Depression Across Several Nations

USA-NCS, United States according to the National Comorbidity Study; USA-ECA, United States according to the Epidemiological Catchment Area Study.

Source: Tsai, J. L., and Chentsova-Dutton, Y. (2002). Understanding depression across cultures." In I. H. Gotlib and C. L. Hammen (Eds.), Handbook of depression (p. 471). The Guilford Press © 2002. Reprinted with permission.

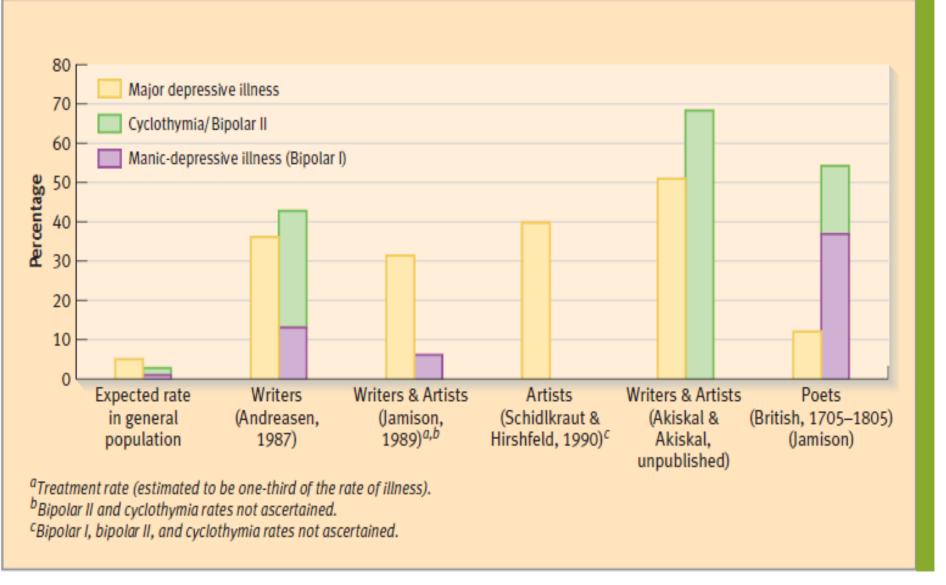


FIGURE 7.9

Rates of Mood Disorders in Writers and Artists

Although it is difficult to determine a reliable diagnosis of influential writers, poets, and artists (many of whom are long ago deceased), a number of psychological historians have compiled figures such as these, which clearly indicate that such individuals are far more likely than the general population to have had a unipolar or bipolar mood disorder. (Adapted from Jamison, K. R., 1993. Touched with fire. Free Press.)

Comorbidity

Table 4. Patterns (cumulative lifetime incidence in %) of longitudinal lifetime (up to age 29 yr) comorbidity in community cases with DSM-IV hypomania, mania and MDD and odds ratio (OR) compared to persons without disorder (Wittchen et al., In Press)

	Hypomania		Mani	Mania		MDD	
Comorbid disorder	%	OR	%	OR	%	OR	
Alcohol	28.7	1.3	54.5	3.5***	32.3	1.7***	
Drugs	12.5	1.9*	17.1	2.3*	12.1	2.3***	
Psychotic	na		na		na		
Phobias	24.7	1.6	33.2	2.7**	28.4	2.5***	
Panic	3.6	1.3	7.4	3.4*	6.8	4.9***	
GAD	4.6	1.6	13.4	6.1	8.4	7.0***	
Agoraphobia	5.7	1.8	17.5	7.9***	6.9	3.4***	
PTSD	3.7	1.9	6.4	4.2*	4.5	4.5***	
OCD	2.8	2.8	12.2	14.6***	1.7	3.0*	
Eating	8.6	1.8*	7.9	2.1	8.6	2.7***	
2+ disorders (from above)	38.8	1.7*	60.4	4.4***	45.4	3.1***	

Wittchen, Hans-Ulrich, Stephan Mühlig, and Lukas Pezawas. "Natural Course and Burden of Bipolar Disorders." *The International Journal of Neuropsychopharmacology Int. J. Neuropsychopharm.* 6.2 (2003): 145-54. Web.

Etiology

Causal Factors in Bipolar Disorder

Biological causal factors

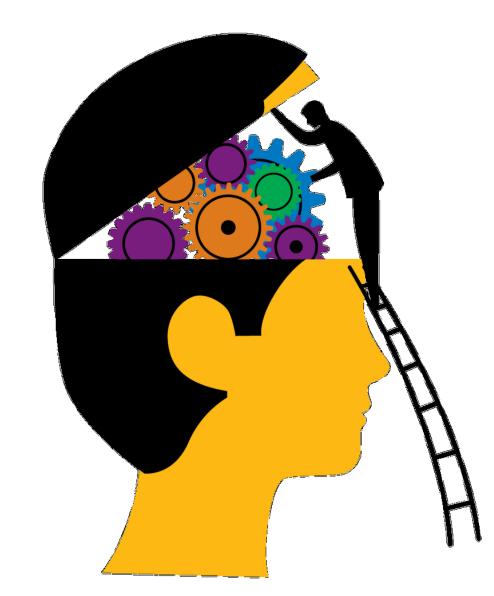
- Genetic factors: 8-10% first degree relatives, twin studies and high concordance (60% in monozygotic, 12% in dizygotic)
- Neurochemical factors: norepinephrine, serotonin, dopamine and high dopamanergic activity
- Hormonal abnormalities: elevated cortisol, thyroid hormones

- Neurological factors: "blood flow to the left prefrontal cortex is reduced during depression, during mania it is increased in certain other parts of the prefrontal cortex (Goodwin & Jamison, 2007)" (Butcher, 246).
- Enlarged basal ganglia and amygdala, reduced volume in hippocampal area
- Biological rhythms: sleep and circadian rhythms



Assessment and Diagnosis

- Interview with the patient
- Interview with the family o relatives
- Observation
- DSM-V Criteria



Treatment

• The important problem!

People usually tend not to seek help

- Relapses
- Public awareness
- People who can get a treatment and people who cannot get a

treatment

Pharmacotheraphy

• 1950: monoamine oxidase inhibitors (MAOIs)

Treating depression but dangerous / sometimes fatal

• 1960-1990: tricyclic antidepressants

Side effects

Selective Serotonin Reuptake Inhibitor (SSRI)

Side effects such as sexual dysfunction

• Lithium

Mood stabilizer

Especially for manic episodes

Better for preventing cycling

Still some side effects: cognitive slowing, weight gain etc.

Panel 2: Long-term treatment of bipolar disorders

Established options, evidence from various controlled studies Possibly efficacious, wideLithium salts Carbamazepine Valproic acid

Possibly efficacious, widespread in clinical practice, limited evidence

Weak evidence

Calcium antagonists

Experimental as monotherapy, limited evidence as adjunct treatment

Anticonvulsants:
Iamotrigine, gabapentine,
topiramate
Thyroid hormones:

Inyroid hormones: levothyroxine Atypical neuroleptics:

clozapine, olanzapine

Panel 3: Treatment of acute mania

Form of manic state Mild, moderate, and euphoric Treatment options

Lithium salts initially combined with benzodiazepines Carbamazepine initially

combined with benzodiazepines

Valproic acid Olanzapine

Severe, incooperative, psychotic, and euphoric

Lithium salts plus antipsychotics
Carbamazepine plus antipsychotics
Valproic acid plus antipsychotics
if necessary

if necessary

Olanzapine plus one mood stabiliser

Mixed or dysphoric type

Valproic acid

Additional somatic complications (cardiac disease, pregnancy)

Electroconvulsive therapy

Refractory mania Electroconvulsive therapy

Panel 4: Treatment of bipolar depression

Depressive state Treatment options

In absence of prophylactic treatment

Mild and moderate Lithium

Interpersonal psychotherapy, cognitive behavioural therapy

Severe Lithium plus antidepressant

Breakthrough depression under prophylactic treatment

Mild and moderate Optimisation of prophylactic treatment

with mood stabiliser

Severe Current mood stabiliser plus selective

serotonin reuptake inhibitors or second

mood stabiliser

Depression in rapid

cycling

Strictly avoid antidepressants

Current mood stabiliser plus second

mood stabiliser

Addition of levothyroxine

Refractory depression Electroconvulsive therapy

Biological Treatments

Electroconvulsive Theraphy

Severe depression, suicidal risks, for people who deny to take medicine etc.

Transcranial Magnetic Stimulation (TMS)

A magnetic coil is placed near the head of the person and it produces small electric signals to the brain region.

Less side effects to the cognitive functioning

Deep Brain Stimulation

A neurostimulator is placed in the specific brain region which sends electrical signals

Bright Light Theraphy

Exposure to daylight or to specific wavelengths of light

Psychotheraphy

"The belief that people with psychological problems can change—can learn more adaptive ways of perceiving, evaluating, and behaving—is the conviction underlying all psychotherapy" (Butcher, 2007).

Cognitive-Behavioral Theraphy

Combination with medication

Behavioral Activation Theraphy

Interpersonal therapy

Family Theraphy

Criticism reduce and its effect on relapses

Cognitive-Behavioral Theraphy

- "A key component addressed in CBT for bipolar depression is the way that the patients deal with the serious losses that experience as a consequence of their bipolar disorder" (Mansell, W., Colom, F., & Scott, J. 2005).
- Changing the negative cognitions
- Activity schedules which encourages the abilities and activities of the patients that they think they are gone

• "In particular, the patient is encouraged to see the benefits of pleasurable behaviour that do not involve large increases in activity and are not directed at achieving highly challenging goals. Having a bath or listening to relaxing music are examples" (Mansell, W., Colom, F., & Scott, J. 2005).

- Brief form of treatment (usually 10 to 20 sessions) which focuses on here and present problems
- Focus on the results of the disorder on the patient's life and well being
- Focus on suicidal risks
- Focus on negative appraisals
- Uses pleasurable relaxing activities
- Relapse prevention

Behavioral Activation Theraphy

- Focuses on helping patients to become more active and become more in interaction with their environment
- Scheduling activities
- Exploring new behavior to reach goals
- Role playing to find out the deficits
- Focuses more on changing the behavior than CBT
- Positive reinforcement and reduced avoidance

- Interpersonal Theraphy:
- Focuses on present relationship problems
- Focuses on changing the maladaptive relation and interaction patterns
- Focuses on stabilizing the daily rhythm and social patterns

Family Theraphy

- Relapses can be triggered by the negative elements in the patient's family life
- Criticism as an element for depression relapse
- Expressed emotions and hostility in the family as a trigger to bipolar relapses

- Family interventions
- Providing information for the family about how to deal with the disorder
- Marital interventions which focus on marital problems in the patient's life and to increase marital satisfaction

Bipolar Disorder in Real Life

Table 1 Studies of independent severe negative life events in bipolar disorder

Author (year)	Sample	n for bipolar group	Life events measure
Alloy et al., 1999	Students with cyclothymia, dysthymia or hypomania	43	LES
Bebbington et al., 1993	Inpatients with psychotic mania	31	revised LEDS
Christensen et al., 2003	BPD patients with at least 3 hospitalizations	56	RLE
Chung et al., 1986	Hypomanic inpatients	14	LEDS
Ellicot et al., 1990	BPD patients receiving medications and remitted	61	Revised LEDS
Hunt et al., 1992	Patients with BPD	62	RLE
Johnson & Miller, 1997	Community residents with BPD	65	LEDS
Johnson et al., 2000	Community residents with BDP	149	LEDS
Johnson et al., 2004	Community residents with BPD	59	LEDS
Kennedy et al., 1983	Inpatients with mania	20	RLE
Malkoff-Schwartz et al., 2000	Manic or cycling participants compared to control participants	45	LEDS
McPherson et al., 1993	Patients with BPD	58	RLE
Pardoen et al., 1996	Patients with recovered BPD	27	RLE
Reilly-Harrington et al., 1999	Students with RDC BP spectrum disorder		LES
Sclare & Creed, 1990	Manic inpatients	24	LEDS

BPD—bipolar disorder. RLE—interview for recent life events. LEDS—life events and difficulties schedule. LES—self-report life events survey followed by interview and ratings.

"My temperament, moods, and illness clearly, and deeply, affected the relationships I had with others and the fabric of my work. But my moods were themselves powerfully shaped by the same relationships and work. The challenge was in learning to understand the complexity of this mutual beholdenness..." (Alloy, 2005).

References

- Alloy, L. B., Abramson, L. Y., Urosevic, S., Walshaw, P. D., Nusslock, R., & Neeren, A.
 M. (2005). The psychosocial context of bipolar disorder: Environmental, cognitive, and developmental risk factors. *Clinical Psychology Review*, 25(8), 1043-1075.
- Butcher, J. N., Mineka, S., & Hooley, J. M. (2007). *Abnormal psychology*. Boston: Pearson/Allyn and Bacon.
- Johnson, S. L. (2005). Life events in bipolar disorder: Towards more specific models. *Clinical Psychology Review, 25*(8), 1008-1027.
- Mansell, W., Colom, F., & Scott, J. (2005). The nature and treatment of depression in bipolar disorder: A review and implications for future psychological investigation. *Clinical Psychology Review, 25*(8), 1076-1100.
- Mendlewicz, J., Souery, D., & Rivelli, S. K. (1999). Short-term and long-term treatment for bipolar patients: Beyond the guidelines. *Journal of Affective Disorders*, 55(1), 79-85.

- Merikangas, K. R., Akiskal, H. S., Angst, J., Greenberg, P. E., Hirschfeld, R. M., Petukhova, M., & Kessler, R. C. (2007). Lifetime and 12-Month Prevalence of Bipolar Spectrum Disorder in the National Comorbidity Survey Replication. *Arch Gen Psychiatry Archives of General Psychiatry*, 64(5), 543.
- Müller-Oerlinghausen, B., Berghöfer, A., & Bauer, M. (2002). Bipolar disorder. *The Lancet*, 359(9302), 241-247.
- Pini, S., Queiroz, V. D., Pagnin, D., Pezawas, L., Angst, J., Cassano, G. B.,
 & Wittchen, H. (2005). Prevalence and burden of bipolar disorders in
 European countries. *European Neuropsychopharmacology*, 15(4), 425-434.
- Wittchen, H., Mühlig, S., & Pezawas, L. (2003). Natural course and burden of bipolar disorders. *The International Journal of Neuropsychopharmacology Int. J. Neuropsychopharm.*, 6(2), 145-154.
- https://www.youtube.com/watch?v=IJtXLXQ326A

Thank you for listening!