Bipolar Disorders

Teaching and Research office of Psychiatry, West China medical school S.U.

Main Points

- General considerations
- Major etiologic theories
- Epidemiology
- Genetics
- Clinical findings
- DSM-Ⅳ diagnostic criteria
- Differential diagnosis
- Treatment
- Course of illness & prognosis

General Considerations

- Bipolar disorders can be conceptualized into three distinct entities:
  - Bipolar Ⅰ disorder, consisting of episodes of mania cycling with depressive episodes;
  - Bipolar Ⅱ disorder, consisting of hypomania cycling with depressive episodes;
  - Cyclothymic disorder, consisting of hypomania and less severe episodes of depression
  - Very few patients have only manic episodes

Major Etiologic Theories

- Despite intensive attempts to establish its etiologic or pathophysiologic basis, the precise cause of bipolar disorders is not known.
- As in major depressive disorder, there is consensus that multiple etiologic factors—genetic, biochemical, psychodynamic, and socioenvironmental—may interact in complex ways.

Major Etiologic Theories

- Life events
  - Although psychosocial stressors can occasionally precede the onset of bipolar disorders, there is no clear association between life events and the onset of manic or hypomanic episodes.

Major Etiologic Theories

- Biological theories
  - Neurotransmitters
    - Neurotransmitter theories initially conceptualized that depression and mania are on the opposite ends of the same continuum.
  - Neuriendocrine factors
    - Abnormalities in the HPA axis and, more so, in the HPT axis are common in bipolar disorder.

Major Etiologic Theories

- Psychosocial theories
  - Psychosocial theories pertaining to the etiology of bipolar disorders are the same as those described for major depressive disorder.
  - Kindling model
    - Environmental conditions contribute more to the timing of a bipolar episode than to the patient's underlying vulnerability.

Epidemiology

- The following table will summarize the relevant risk factors.

Risk factors for bipolar disorders

Social class	Found more frequently in the upper socioeconomic class
Race	No relationship
Life events	No relationship
Personality	No relationship
Childhood experience	No relationship
Marital status	Data not uniform
Family history	Bipolar patients have both bipolar and unipolat first-degree relatives in roughly equal proportions

Epidemiology

- Among the key risk factors for BPD are being female, having a family history of BPD, and coming from an upper socioeconomic class.

- Data also suggest that people under age 50 years are at higher risk of a first attack of BPD, whereas someone who already has disorder faces an increasing risk of a recurrent manic or depressive episode as he/she grows older.

Epidemiology

- Epidemiologic Catchment Area (ECA) studies support a lifetime prevalence of BPD ranging from 0.6 to 1.1% (male:0.8-1.1%, female:0.5-1.3%).
- The disorder affects over 3 million persons in the US.
- It accounts for one quarter of all mood disorders.
- It is likely that prevalence rates of BPD are underestimated, because of problems in identifying manic and, more so, hypomanic episodes.

Epidemiology

- Approximately 10-15% of adolescents with recurrent major depression will go on to develop bipolar Ⅰ disorder.
- Mixed episodes appear to be more likely in adolescents and young adults than in older adults.
- An age at onset for a first manic episode after age 40 years should alter the clinician to the possibility that the symptoms may due to a general medical condition or substance use.
- Patients with early-onset BPD are more likely to display psychotic symptoms and to have a poorer prognosis in terms of lifetime outcome.

Epidemiology

- Mood disorders often have seasonal patterns. Acute episodes of depression are common in spring and fall, whereas mania appears to cluster in the summer months.

Genetics

- Twin and family studies provide strong evidence for a genetic component in BPD, but the precise mechanisms of inheritance are not known.
- In dizygotic twins, concordance rates are 24% for BPD and 19% for unipolar disorder.
- In monozygotic twins, the concordance rate is higher for BPD (80%) than for unipolar disorder (54%).
- Adoption studies have shown that the biological children of affected parents have an increased risk for developing a mood disorder, even when reared by unaffected parents, although the data are not uniform.

Genetics

- Adoption studies have shown that the biological children of affected parents have an increased risk for developing a mood disorder, even when reared by unaffected parents, although the data are not uniform.
- First-degree biological relatives of bipolar Ⅰ patients have elevated rates of bipolar Ⅰ disorder (4-20%), bipolar Ⅱ disorder (1-5%), and major depressive disorder (4-24%)

Clinical Findings

- Signs and Symptoms
  - BPD can be subdivided into two diagnostic entities: bipolar Ⅰ disorder (recurrent major depressive episodes with manic episodes) and bipolar Ⅱ disorder (recurrent major depressive episodes with hypomanic episodes).
  - The symptoms of both BPD involve changes in mood, cognition, and behavior.

Stages of mania

	Stage I	Stage II	Stage III
Mood	Labile affect; euphoria, predominates; irritability if demands not satisfied.	Increased dysphoria and depression; open hostility and anger	Very dysphoric; panic-stricken; hopeless
Cognition	Expansive, grandiose, overconfident; thoughts coherent but occasionally tangential; sexual and religious preoccupation; racing thoughts	Flight of ideas; disorganization of cognition; delusions	Incoherent, definite loosening of associations; bizarre and idiosyncratic delusions; hallucinations in one third of patients; disorientation to time and place; occasional ideas of refernce
Behavior	Increased psychomotor activity; increased rate of speech; increased spending, smoking, telephone use	Increased psychomotor activity; pressured speech; occasional assaultive behavior	Frenzied, frequently bizarre psychomotor activity

Signs and Symptoms

- Bipolar Ⅰ disorder
  - Episodes typically begin suddenly, with a rapid escalation through the stages summarized in previous table.
  - In 50-60% of cases, a depressive episode immediately precedes or follows a manic episode. The hallmark of a manic episode is abnormally and persistently elevated, expansive, or irritable mood.

Signs and Symptoms

- Bipolar Ⅰ disorder
  - Somatic features
    - Bipolar patients' sleep varies with their clinical state. As the manic episode intensifies, patients may go without sleep for nights, their insomnia further intensifying the manic syndrome.
    - There is a speculation as to whether the insomnia precedes, and perhaps triggers or fuels, the manic episode.

Signs and Symptoms

- Bipolar Ⅰ disorder
  - Behavioral features
    - Patients are initially social, outgoing, self confident, and can be difficult to interrupt. Their speech is full of puns, jokes, and irrelevancies.
    - Patients are often hypersexual, promiscuous, disinhibited, and seductive; they may present to an emergency room setting dressed in colorful, flamboyant, and inappropriate clothing.
    - As the manic episode intensifies, their speech becomes loud, intrusive, rapid, and difficult to follow, and they can become irritable, assaultive, and threatening.

Signs and Symptoms

- Bipolar Ⅰ disorder
  - Cognitive features
    - Manic patients are easily distracted. Their thought processes are difficult to follow because of racing thoughts and flight of ideas.
    - They appear to have an unrestrained and accelerated flow of thoughts and ideas, which are often unrelated.
    - Patients can be overly self-confident and become preoccupied with political, personal, religious, and sexual themes. They may exhibit an inappropriate increase in self-esteem and open grandiosity.
    - Their judgment is impaired significantly, resulting in buying sprees, sexual indiscretions, and unwise business investments.
    - Psycho features such as paranoia, delusions, and hallucinations are often present, not unlike those seen in patients with schizophrenia.

Signs and Symptoms

- Bipolar Ⅰ disorder
  - Risk of suicide
    - Bipolar patients are at a substantial risk for suicide, with a mortality rate 2-3 times higher than the general population.
    - Risk factors for suicide among bipolar patients include previous suicide attempts, co-morbid substance abuse, a mixed episode, current depressive episode, and a history of rapid-cycling bipolar disorder.

Signs and Symptoms

- Bipolar Ⅱ disorder
  - Characterized by recurrent episodes of major depression and hypomania, it has been identified as a distinct disorder only in DSM-Ⅳ.
  - Hypomania symptoms are similar to manic symptoms but typically do not reach the same level of symptom severity or social impairment
  - Hypomania does not usually present with psychotic symptoms, racing thoughts, or marked psychomotor agitation.
  - Hypomania patients do not perceive themselves as being ill and are likely to minimize their symptoms and to resist treatment.

Signs and Symptoms

- Rapid-cycling bipolar disorder
  - Patients with rapid-cycling bipolar disorder experience four or more affective episodes per year.
  - Approximately 10-15% of bipolar patients experience rapid cycling.
  - Although similar to other bipolar patients nosologically and demographically, patients with rapid-cycling bipolar disorder tend to have a longer duration of illness, and the illness has a more refractory course.

Signs and Symptoms

- Rapid-cycling bipolar disorder
  - Women are represented disproportionately, making up 80-95% of rapid-cycling patients.
  - A variety of factors may predispose bipolar illness to a rapid-cycling course, including treatment with TCAs, MAOIs, lithium, and antipsychotics.
  - The development of clinical or subclinical hypothyroidism (spontaneously or during lithium treatment) in a manic patient predispose to a more rapidly cycling course.
  - The kindling hypothesis, invoked to conceptualize these changes pathophysiologically, receives further confirmation by clinical usefulness of the anticonvulsants valproic acid and carbamazepine.

Clinical Findings

- Laboratory Findings and Imaging
  - No laboratory findings are diagnostic of a BPD or of a manic or hypomanic episode. Several laboratory findings have been noted to be abnormal in groups of individuals with BPD. Research findings in BPD are in general scarce and inconclusive.

Laboratory Findings and Imaging

- Hypothalamic-pituitary-adrenal axis
  - The few available cross-sectional and longitudinal studies reveal increased plasma cortisol levels in some depressed bipolar patients.
  - Abnormalities in the DST have also been noted. DST nonsuppression occurs more frequently in bipolar depression and mania.
  - Both hypercortisolemia and DST results normalize after the acute episode subsides, suggesting that these abnormalities are not state and not trait dependent.
  - Although these abnormalities are not specific for BPD or even MD, their pathophysiology is suggestive of central (ie, hypothalamic) rather than peripheral dysregulation of cortisol.

Laboratory Findings and Imaging

- Hypothalamic-pituitary-thyroid axis
  - HPT axis abnormalities are rather common in BPD, especially in rapid-cycling BPD, but the precise relationship of these abnormalities with the illness and its various clinical presentations is not known.
  - There are intriguing associations among thyroid function, BPD, and gender. Hypothyroidism is very common in patients with BPD; it is especially common in female patients who present with rapid-cycling course. Treatment with hypermetabolic doses of T_4 has shown some promise in that it may reduce acute symptoms, number of relapses, and duration of hospitalizations.

Laboratory Findings and Imaging

- Hypothalamic-pituitary-thyroid axis
  - Conceptually some findings support the hypothesis that a relative central thyroid hormone deficit may predispose to the marked and frequent mood swings that characterize rapid-cycling BPD.

Laboratory Findings and Imaging

- Sleep electroencephalogram
  - Sleep EEG recording have revealed normal results in acutely ill bipolar patients, including normal REM latencies, but not all studies agree.
- Brain imaging
  - Patients with right frontotemporal or left parieto-occipital lesions are especially vulnerable to mania or hypomania.

DSM-Ⅳ Diagnostic Criteria

- Manic Episode
  - A distinct period of abnormally and persistently elevated, expansive, or irritable mood lasting at least 1 week (or any duration if hospitalization is necessary).

DSM-Ⅳ Diagnostic Criteria

- Manic Episode
  - During the period of mood disturbance, three (or more) of the following symptoms have persisted (four if the mood is only irritable) and have been present to a significant degree:
    - Inflated self-eteem or grandiosity
    - Decreased need for sleep (eg, feels rested after only 3 hours of sleep)
    - More talkative than usual or pressure to keep talking
    - Flight of ideas or subjective experience that thoughts are racing
    - Distractibility (ie, attention too easily drawn to unimportant or irrelevant external stimuli)
    - Increase in goal-directed activity (either socially, at work or school, or sexually) or psychomotor agitation
    - Excessive involvement in pleasurable activities that have a high potential for painful consequences (eg, engaging in unrestrained buying sprees, sexual indiscretions, or foolish business investments)

DSM-Ⅳ Diagnostic Criteria

- Manic Episode
  - The symptoms do not meet the criteria for a mixed episode.
  - The mood disturbance is sufficiently severe to cause marked impairment in occupational functioning or in usual social activities or relationships with others, or to necessitate hospitalization to prevent harm to self or others, or there are psychotic features.

DSM-Ⅳ Diagnostic Criteria

- Manic Episode
  - The symptoms are not due to the direct physiological effects of a substance (eg, a drug of abuse, a medication, or other treatment) or a general medical condition (eg, hyperthyroidism).
- Note: manic-like episode that are clearly caused by somatic antidepressant treatment (eg, medication, electroconvulsive treatment, light therapy) should not count toward a diagnosis of bipolar Ⅰ disorder.

Differential Diagnosis

- Medical Disorders
  - Numerous medical disorders and medications can induce or mimic the clinical picture of BPD, exacerbate its course and severity, or complicate its treatment.
  - DSM-Ⅳcriteria specify that to make a diagnosis of BPD, the symptoms cannot be the direct result of a substance or a general medical conditions.
  - A late onset of the first manic episode (over age 50) should prompt the clinician to carefully exclude a possible medical cause.

Organic cause of mania and hypomania

Medications

Anticonvulsants
Barbiturates
Benzodiazepines
Bromide
Bronchodilators
Calcium replacement
Cimetidine
Cocaine
Corticosteroids and adrenocorticotropic hormone
Decongestants
Disulfiram
L-Dopa
Hallucinogens
Isoniazid
Metaclopramide
Phencyclidine
Procarbazine
Procyclidine
Sympathomimetic amnes
Tricyclic antidepressants

Metabolic disturbances

Addison's disease
Dialysis
Hemodialysis
Hyperthyroidism
Iatrogenic cushing's disease
Postinfection states
Postoperative states
Vitamin B_{12}

Neurologic disorders

Huntington's disease
Multiple sclerosis
Poststroke
Right hemisphere damage
Right temporal lobe seizure
Seizure disorders

Infectious diseases

Herpes simplex encephalitis
HIV infection
Influenza
Neurosyphilis
Q fever

Neoplasms

Diencephalic glioma
Parasagittal meningioma
Right intraventricular meningioma
Right temporoparietal occipital metastases
Suprasellar craniopharyngioma
Tumor of floor of the forth ventricle

Other conditions

Delirium
Post-ECT
Postisolation syndrome
Posttraumatic confusion
Right temporal lobectomy
Serotonin syndrome

Differential Diagnosis

- Psychiatric Disorders
  - First, the psychotic features associated with schizophrenia or schizoaffective disorder are often indistinguishable from those associated with acute mania.
  - Second, major depressive episodes may be associated prominently with irritable mood and may thus be difficult to distinguish from a mixed bipolar episode.
  - Third, in children and adolescents, ADHD and mania are both characterized by overactivity, impulsive behavior, poor judgment and academic performance, and psychological denial.

Differential Diagnosis

- Psychiatric Disorders
  - Fourth, patients with certain personality disorders (eg, borderline or histrionic personality disorders) can exhibit impulsive, affective instability, and paranoid ideations, as do manic patients.
  - Finally, substance abuse is exceedingly common in patients with BPD. Careful etiologic evaluation, and a drug-free washout period after intoxication, are often necessary to distinguish whether the mood disturbance is the consequence of substance abuse or whether the substance abuse is the consequence of a mood disturbance.

Treatment

- Acute bipolar episodes usually demand immediate symptom containment, which is achieved, most easily using pharmacologic means.

Treatment

- Acute depressive episodes are treated best with SSRIs or bupropion, because these medications are less likely to trigger the switch into mania or hypomania frequently caused by TCAs.
- Acute manic episodes can be managed with lithium, valproic acid, or carbamazepine.
- If delusional symptoms and agitation are present, antipsychotics (eg, haloperidol) or benzodiazepine (eg, clonazepam) need to be added.

Treatment

- Maintenance treatment of BPD, aimed at course stabilization and prevention of further episodes, includes lithium, valproic acid, or carbamazepine.
- Most patients are likely to receive a combination of drugs (eg, lithium, valproic acid or carbamazepine) rather than monotherapy.

Treatment

- Other general treatment principles include mood charting, optimizing sleep, and eliminating mood destabilizers.

Treatment

- Psychotherapy
  - Little is known about the role of psychotherapy in the treatment of BPD.
  - Efforts are currently under way to evaluate whether treatments such as interpersonal psychotherapy or cognitive therapy work as well in bipolar patients as they do in unipolar patients.

Treatment

- Psychotherapy
  - Preliminary evidence indicates that family education may reduce the risk for relapse and that cognitive therapy may enhance compliance with medications.
  - On the whole, some of the newer psychosocial interventions appear to represent a viable alternative or valuable adjunct to pharmacotherapy in mild to moderate unipolar disorder.

Treatment

- Electroconvulsive Therapy
  - Approximately 80% of manic patients show substantial improvement after ECT
  - ECT has proven especially useful for those manic patients who did not respond to medication and for those in mixed states who present with a high risk of suicide and are thus in need of acute symptom containment.

Course of Illness & Prognosis

- Patients usually experience their first manic episode in the early 20s, but BPD sometimes start in adolescence or after age 40 years.
- Manic episodes typically begin suddenly, with a rapid escalation of symptoms over a few days; often they are triggered by psychosocial stressors.
- In about 50% of patients a depressive episode immediately precedes a manic episode.

Course of Illness & Prognosis

- It appears that the availability of treatment for BPD has significantly affected the length of an average episode.
- With the emergence of early intervention and successful treatment of the illness, the effects of kindling on outcome may have been interrupted, resulting in fewer episodes over time and reduced cycle length.
- Early disease onset suggests poor prognosis; patients who experience their initial episode in their late teens are likely to have a less favorable outcome than patients who experience their initial episode in their early 30s.

Course of Illness & Prognosis

- Although medications are effective in treating acute episodes and in maintaining patients in remission, they are not completely effective in preventing future episodes.
- Combinations of lithium and anticonvulsants have shown promise in maintaining euthymia and increasing cycle intervals.

Course of Illness & Prognosis

- Comorbidity with substance abuse, antisocial behavior, and personality disorders often complicates the clinical outcome.
- Substantial psychosocial morbidity can affect marriage, children, occupation, and other aspects of the patient's life.
- Completed suicide rates approximate 15% in bipolar patients, and suicide is more common among females and is usually associated with depressive or mixed episode.