English Teachers On Call

Bipolar Disorders

http://cobbersonthebrain.areavoices.com/2012/11/12/bipolar-disorder-a-disorder-with-no-face/

Bipolar disorders *are characterized by episodes of mania and depression, which may alternate, although many patients have a predominance of one or the other. Exact cause is unknown, but heredity, changes in the level of brain neurotransmitters, and psychosocial factors may be involved. Diagnosis is based on history. Treatment consists of mood-stabilizing drugs, sometimes with psychotherapy.*

Bipolar disorders usually begin in the teens, 20s, or 30s. Lifetime prevalence is about 4%. Rates are about equal for men and women.

Bipolar disorders are classified as

- Bipolar I disorder: Defined by the presence of at least one **full-fledged** (ie, disrupting normal social and occupational function) manic or mixed episode and usually depressive episodes

- Bipolar II disorder: Defined by the presence of major depressive episodes with at least one hypomanic episode but no full-fledged manic episodes
- Bipolar disorder not otherwise specified (NOS): Disorders with clear bipolar features that do not meet the specific criteria for other bipolar disorders

Etiology

Exact cause is unknown. Heredity plays a significant role. There is also evidence of dysregulation of serotonin and norepinephrine. Psychosocial factors may be involved. Stressful life events are often associated with initial development of symptoms and later exacerbations, although cause and effect have not been established. Certain drugs can trigger exacerbations in some patients with bipolar disorder; these drugs include sympathomimetics (eg, cocaine, amphetamines), alcohol, and certain antidepressants (eg, tricyclics, MAOIs).

Symptoms and Signs

Bipolar disorder begins with an acute phase of symptoms, followed by a repeating course of remission and relapse. Remissions are usually complete, although some patients have residual symptoms. Relapses are discrete episodes of more intense symptoms that are manic, depressive, hypomanic, or a mixture of depressive and manic features. Episodes last anywhere from a few weeks to 3 to 6 mo. Cycles—time from onset of one episode to that of the next—vary in length among patients. Some patients have infrequent episodes, perhaps only a few over a lifetime, whereas others have rapid-cycling forms (usually defined as ≥ 4 episodes/yr). Only a minority alternate back and forth between mania and depression with each cycle; in most, one or the other predominates to some extent.

Mania: A manic episode is defined as ≥ 1 wk of a persistently elevated, expansive, or irritable mood plus ≥ 3 additional symptoms:

- Inflated self-esteem or grandiosity
- Decreased need for sleep
- Greater talkativeness than usual
- Persistent elevation of mood

- Flight of ideas or racing of thoughts
- Distractibility
- Increased goal-directed activity

http://www.personal.psu.edu/afr3/blogs/SIOW/2011/12/bipolar-disorder.html

Manic patients are inexhaustibly, excessively, and impulsively involved in various pleasurable, high-risk activities (eg, gambling, dangerous sports, promiscuous sexual activity) without insight into possible harm. Symptoms are so severe that they impair functioning; unwise investments, spending sprees, and other personal choices may have irreparable consequences.

Typically, patients in a manic episode are exuberant and flamboyantly or colorfully dressed; they have an authoritative manner with a rapid, unstoppable flow of speech. Patients may make clang associations (new thoughts that are triggered by word sounds rather than meaning). Easily distracted, patients may constantly shift from one theme or endeavor to another. However, they tend to

believe they are in their best mental state. Lack of insight and an increased capacity for activity often lead to intrusive behavior and can be a dangerous combination. Interpersonal friction results and may cause patients to feel that they are being unjustly treated or persecuted. As a result, patients may become a danger to themselves or to other people. Accelerated mental activity is experienced as racing thoughts by patients and is observed as flights of ideas by the physician.

Manic psychosis is a more extreme manifestation, with psychotic symptoms that may be difficult to distinguish from schizophrenia. Patients may have extreme grandiose or persecutory delusions (eg, of being Jesus or being pursued by the FBI), occasionally with hallucinations. Activity level increases markedly; patients may race about and scream, swear, or sing. Mood lability increases, often with increasing irritability. Full-blown delirium (delirious mania) may appear, with complete loss of coherent thinking and behavior.

Hypomania: A hypomanic episode is a less extreme variant of mania involving a distinct episode that lasts ≥ 4 days and is distinctly different from the patient's usual non-depressed mood. During the hypomanic period, mood brightens, the need for sleep decreases, and psychomotor activity accelerates. For some patients, hypomanic periods are adaptive because they produce high energy, creativity, confidence, and supernormal social functioning. Many do not wish to leave the pleasurable, euphoric state. Some function quite well, and in most, functioning is not markedly impaired. However, in some patients, hypomania manifests as distractibility, irritability, and labile mood, which the patient and others find less attractive.

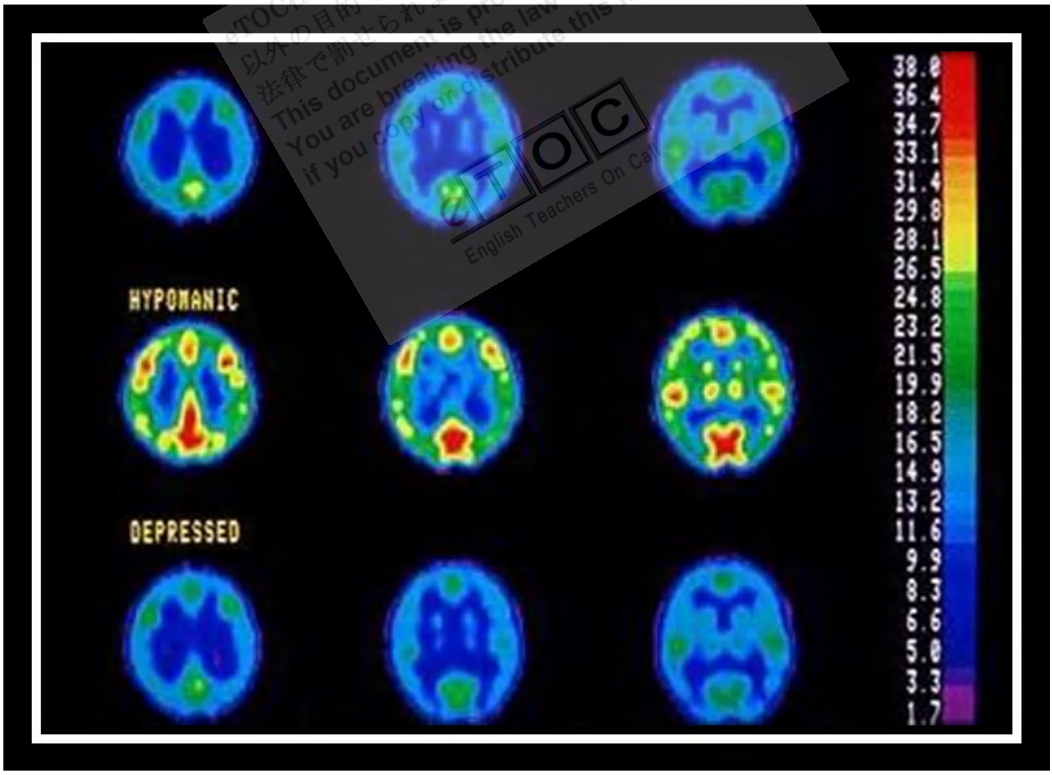
Depression: A depressive episode has features typical of major depression, including depressed mood, anhedonia, psychomotor retardation, and feelings of pessimism and guilt. Sleeping and eating often increase. Delusions of guilt accompanied by self-loathing are common in psychotic depression, and some patients have hallucinations.

Mixed state: A mixed episode blends depressive and manic or hypomanic features; the criteria for both mania and depression are met. For example, patients may momentarily switch to tearfulness during the height of mania, or

their thoughts may race during a depressive period. Often, the switch follows circadian factors (eg, going to bed depressed and waking early in the morning in a hypomanic state). In at least one third of people with bipolar disorder, the entire episode is mixed. A common presentation consists of a dysphorically excited mood, crying, curtailed sleep, racing thoughts, grandiosity, psychomotor restlessness, suicidal ideation, persecutory delusions, auditory hallucinations, indecisiveness, and confusion. This presentation is called dysphoric mania (ie, prominent depressive symptoms superimposed on manic psychosis).

Diagnosis

- Clinical criteria (*Diagnostic and Statistical Manual of Mental Disorders*, Fourth Edition Text Revision)
- Thyroxine (T_4) and thyroid-stimulating hormone (TSH) levels to exclude hyperthyroidism
- Exclusion of stimulant drug abuse clinically or by urine testing



http://www.medicalook.com/Neurological_disorders/Bipolar_disorder.html

Diagnosis is based on identification of symptoms of mania or hypomania as described above, plus a history of remission and relapse. Some patients who present with depressive symptoms may have previously experienced hypomania or mania but do not report it unless they are specifically questioned. Skillful questioning may reveal morbid signs (eg, excesses in spending, impulsive sexual escapades, stimulant drug abuse), although such information is more likely to be provided by relatives. All patients must be asked gently but directly about suicidal ideation, plans, or activity.

Similar acute manic or hypomanic symptoms may result from stimulant abuse, a schizoaffective disorder (bipolar type), or physical disorders such as hyperthyroidism or pheochromocytoma. A review of substance use (especially of amphetamines and cocaine) and urine drug screening can help identify drug causes. However, because drug use may simply have triggered an episode in a patient with bipolar disorder, seeking evidence of symptoms (manic or depressive) not related to drug use is important. Patients with a schizoaffective disorder rarely return to normal between episodes, and they do not show the interest in connecting with other people manifested by patients with mania (except those with the most florid type). Patients with hyperthyroidism typically have other physical symptoms and signs, but thyroid function testing (T_4 and TSH levels) is a reasonable screen for new patients. Patients with pheochromocytoma are markedly hypertensive; if not, testing is not indicated.

Patients with bipolar disorder may also have anxiety disorders (eg, social phobia, panic attacks, obsessive-compulsive disorders), possibly confusing the diagnosis.

Treatment

- Mood stabilizers (eg, lithium, certain anticonvulsants), a 2nd-generation antipsychotic, or both
- Support and psychotherapy

Treatment usually has 3 phases:

- Acute: To stabilize and control the initial, sometimes severe manifestations
- Continuation: To attain full remission

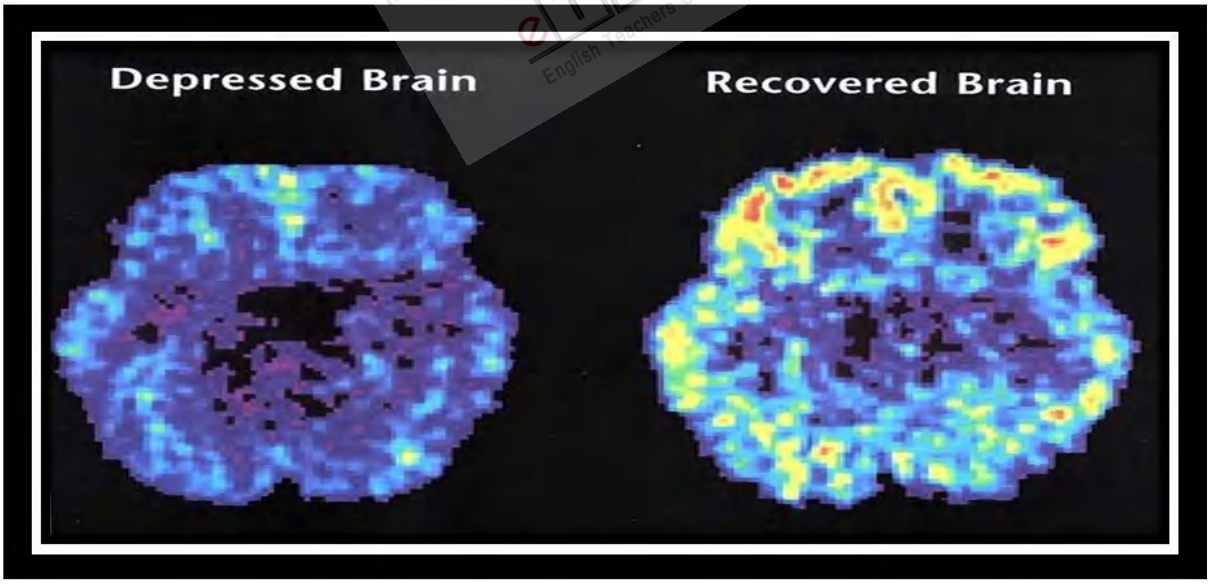
- Maintenance or prevention: To keep patients in remission

Although most patients with hypomania can be treated as outpatients, severe mania or depression often requires inpatient management.

Drugs for bipolar disorder include mood stabilizers and 2nd-generation antipsychotics. These drugs are used alone or in combination for all phases of treatment, although at different dosages.

Mood stabilizers consist of lithium and certain anticonvulsants, especially valproa, carbamazepine, and lamotrigine. Second-generation antipsychotics includearipiprazole, olanzapine, quetiapine, risperidone, and ziprasidone. Specific antidepressants (eg, SSRIs) are sometimes added for severe depression, but antidepressants (particularly heterocyclics) may trigger mania, and their effectiveness continues to be studied. They are not recommended as sole therapy for depressive episodes.

Electroconvulsive therapy (ECT) is sometimes used for depression refractory to treatment and is also effective for mania. Phototherapy can be useful in treating seasonal bipolar I or bipolar II disorder (with autumn-winter depression and spring-summer hypomania). It is probably most useful as augmentative therapy.



http://www.geronguide.com/gallery/index.php/Bipolar-Disorder/bipolar-disorder-causes-03

Drug selection and use: Choice of drug can be difficult because all drugs have significant adverse effects, drug interactions are common, and no drug is

universally effective. Selection should be based on what has previously been effective and well tolerated in a given patient. If there is no prior experience (or it is unknown), choice is based on the patient's medical history (vis-à-vis the adverse effects of the specific mood stabilizer) and the severity of symptoms.

For severe manic psychosis, in which immediate patient safety and management is compromised, urgent behavioral control usually requires a sedating 2nd-generation antipsychotic, sometimes supplemented initially with a benzodiazepine such as lorazepam or clonazepam 2 to 4 mg IM or po tid.

For less severe acute episodes in patients without contraindications (eg, renal disorders),lithium is a good first choice for both mania and depressive episodes. Because its onset is slow (4 to 10 days), patients with significant symptoms may also be given an anticonvulsant or a 2nd-generation antipsychotic. For those with depression, lamotrigine may be a good choice of anticonvulsant.

Once remission is achieved, preventive treatment with mood stabilizers is indicated for all bipolar I patients. If episodes recur during maintenance treatment, clinicians should determine whether adherence is poor and, if so, whether non-adherence preceded or followed recurrence. Reasons for non-adherence should be explored to determine whether a change in mood stabilizer type or dosing would render treatment more acceptable.

Lithium: As many as two thirds of patients with uncomplicated bipolar disorder may respond to lithium, which attenuates bipolar mood swings but has no effect on normal mood. Whether lithium or another mood stabilizer is being used, breakthroughs are more likely in patients who have mixed states, rapid-cycling forms of bipolar disorder, comorbid anxiety, substance abuse, or a neurologic disorder.

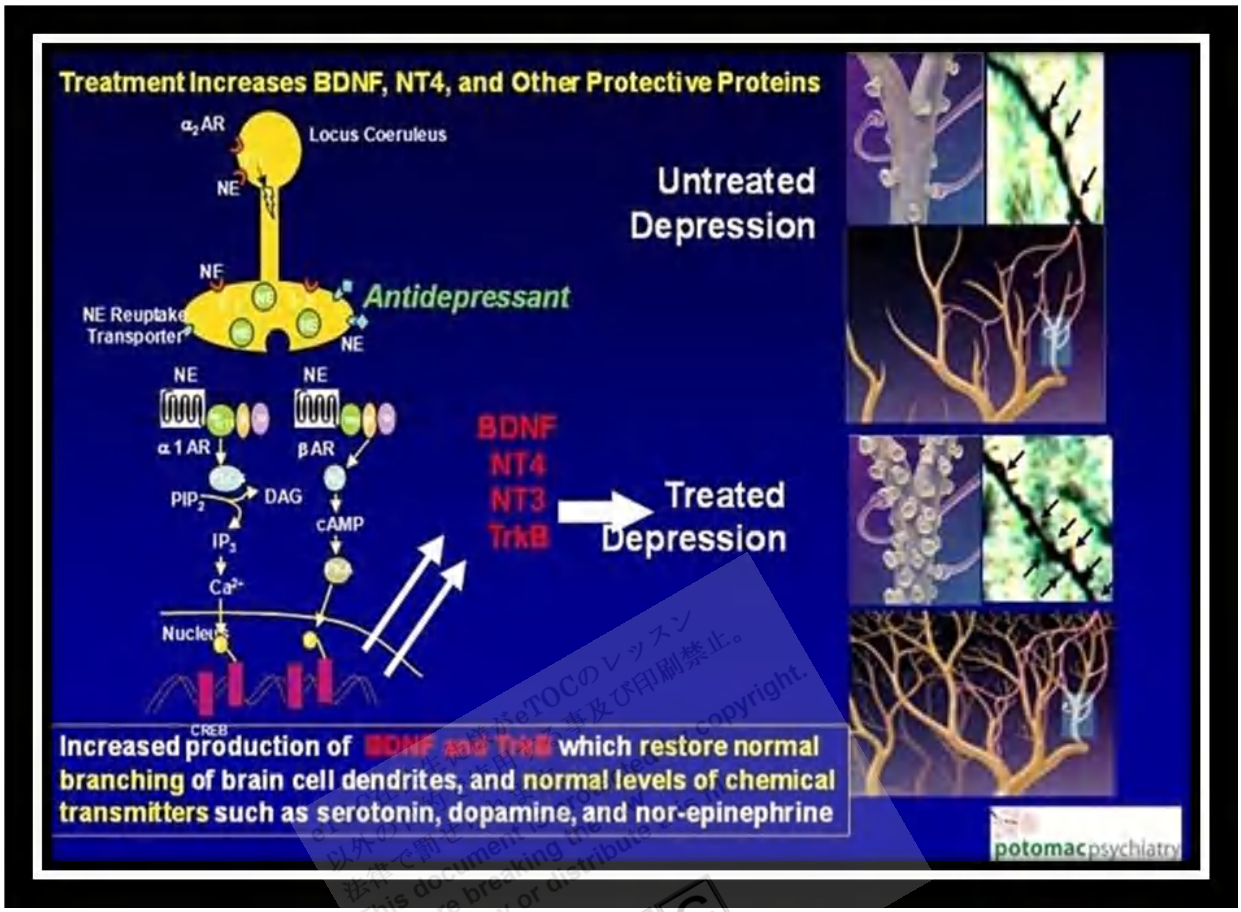
Lithium carbonate is started at 300 mg po bid or tid and titrated, based on steady-state blood levels and tolerance, to a range of 0.8 to 1.2 mEq/L. Levels should be drawn after 5 days at a stable dose and 12 h after the last dose. Target drug levels for maintenance are lower, about 0.6 to 0.7 mEq/L. Higher maintenance levels are more protective against manic (but not depressive)

episodes but have more adverse effects. Adolescents, whose glomerular function is excellent, need higher doses; elderly patients need lower doses.

Lithium can cause sedation and cognitive impairment directly or indirectly (by causing hypothyroidism) and often exacerbates acne and **psoriasis**. The most common acute, mild adverse effects are fine tremor, **fasciculation**, nausea, diarrhea, **polyuria**, **polydipsia**, and weight gain (partly attributed to drinking high-calorie beverages). These effects are usually transient and often respond to decreasing the dose slightly, dividing the dose (eg, tid), or using slow-release forms. Once dosage is established, the entire dose should be given after the evening meal. This dosing may improve adherence. A β-blocker (eg, atenolol 25 to 50 mg po once/day) can control severe tremor; however, some β-blockers (eg, propranolol) may worsen depression.

Acute lithium toxicity is manifested initially by gross tremor, increased deep tendon reflexes, persistent headache, vomiting, and confusion and may progress to stupor, seizures, and **arrhythmias**. Toxicity is more likely to occur in elderly patients, in patients with decreased creatinine clearance, and in those with Na loss (eg, due to fever, vomiting, diarrhea, or use of diuretics). Thiazide diuretics, ACE inhibitors, and NSAIDs other than aspirin may contribute to **hyperlithemia**. Lithium blood levels should be measured every 6 mo and whenever the dose is changed.

Long-term effects include hypothyroidism, particularly when there is a family history of hypothyroidism, and renal damage involving the **distal tubule** (mainly in patients with a history of renal parenchymal disease). Therefore, TSH levels should be monitored when lithium is started and annually thereafter if there is a family history of thyroid dysfunction or every other year for all other patients. Levels should also be measured whenever symptoms suggest thyroid dysfunction (including when mania recurs) because hypothyroidism may blunt the effect of mood stabilizers. BUN and creatinine should be measured at baseline, 2 or 3 times during the first 6 mo, and then once or twice a year.



http://www.geronguide.com/gallery/index.php/Bipolar-Disorder/bipolar-disorder-causes-05

Anticonvulsants: Anticonvulsants that act as mood stabilizers, especially valproate andcarbamazepine, are often used for acute mania and for mixed states (mania and depression). Lamotrigine is also effective for mood-cycling and for depression; unlike some antidepressants, it does not induce mania. The precise mechanism of action for anticonvulsants in bipolar disorder is unknown but may involve γ-aminobutyric acid mechanisms and ultimately G-protein signaling systems. Their main advantages overlithium include a wider therapeutic margin and lack of renal toxicity.

For valproate, a loading dose of 20 mg/kg is given, then 250 to 500 mg po tid (extended-release formulation can be used); target blood levels are between 50 and 125 µg/mL. Adverse effects include nausea, headache, sedation, dizziness, and weight gain; rare serious effects include hepatotoxicity and pancreatitis.

Carbamazepine should not be loaded; it should be started at 200 mg po bid and be increased gradually in 200-mg/day increments to target levels between 4 and 12 µg/mL (maximum, 800 mg bid). Adverse effects include nausea, dizziness, sedation, and unsteadiness. Very severe effects include aplastic anemia and agranulocytosis.

Lamotrigine is started at 25 mg po once/day for 2 wk, then 50 mg once/day for 2 wk, then 100 mg/day for 1 wk, and then can be increased by 50 mg each week as needed up to 200 mg once/day. Dosage is lower for patients taking valproate and higher for patients takingcarbamazepine. Lamotrigine can cause rash and, rarely, the life-threatening Stevens-Johnson syndrome, particularly if the dosage is increased more rapidly than recommended. While taking lamotrigine, patients should be encouraged to report any new rash, hives, fever, swollen glands, sores in the mouth and on the eyes, and swelling of the lips or tongue.

Antipsychotics: Acute manic psychosis is being increasingly managed with 2nd-generation antipsychotics, such as risperidone (usually 4 to 6 mg po once/day), olanzapine (usually 10 to 20 mg po once/day), quetiapine (200 to 400 mg po bid), ziprasidone (40 to 80 mg po bid), and aripiprazole (10 to 30 mg po once/day). In addition, evidence suggests that these drugs may enhance the effects of mood stabilizers after the acute phase.

Although any of these drugs may have extrapyramidal adverse effects and cause akathisia, risk is lower with more sedating drugs such as quetiapine and olanzapine. Less immediate adverse effects include substantial weight gain and development of the metabolic syndrome (including weight gain, excess abdominal fat, insulin resistance, and dyslipidemia); risk may be lower with the least sedating 2nd-generation antipsychotics, ziprasidone andaripiprazole. For extremely hyperactive psychotic patients with poor food and fluid intake, an antipsychotic given IM plus supportive care in addition to lithium or an anticonvulsant may be appropriate.

Precautions during pregnancy: Lithium use during pregnancy has been associated with an increased risk of cardiovascular malformations (particularly Ebstein's anomaly). However, the absolute risk of this particular malformation is

quite low. Taking lithium during pregnancy appears to increase the relative risk of any congenital anomaly by about 2-fold, a risk similar to the 2- to 3-fold increased risk of congenital anomalies associated with use of carbamazepine or lamotrigine and is substantially lower than the risk associated with use of valproate.

Extensive study of the use of 1st-generation antipsychotics and tricyclic antidepressants during early pregnancy has not revealed causes for concern. The same appears to be true of SSRIs, except for paroxetine. Data about the risks of 2nd-generation antipsychotics to the fetus are sparse as yet, even though these drugs are being more widely used for all phases of bipolar disorder.

Use of drugs (particularly lithium and SSRIs) before parturition may have carry-over effects on neonates.

Treatment decisions are complicated by the fact that with unplanned pregnancy, teratogenic effects may already have taken place by the time practitioners' become aware of the issue. Consultation with a perinatal psychiatrist should be considered. In all cases, discussing the risks and benefits of treatment with patients is important.

Education and psychotherapy: Enlisting the support of loved ones is crucial to preventing major episodes. Group therapy is often recommended for patients and their partner; there, they learn about bipolar disorder, its social sequelae, and the central role of mood stabilizers in treatment. Individual psychotherapy may help patients better cope with problems of daily living and adjust to a new way of identifying themselves.

Patients, particularly those with bipolar II disorder, may not adhere to mood-stabilizer regimens because they believe that these drugs make them less alert and creative. The physician can explain that decreased creativity is relatively uncommon because mood stabilizers usually provide opportunity for a more even performance in interpersonal, scholastic, professional, and artistic pursuits.

Patients should be counseled to avoid stimulant drugs and alcohol, to minimize sleep deprivation, and to recognize early signs of relapse. If patients tend to be financially extravagant, finances should be turned over to a trusted family member. Patients with a tendency to sexual excesses should be given information about conjugal consequences (eg, divorce) and infectious risks of promiscuity, particularly AIDS.

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Reference: http://www.merckmanuals.com