



# BIPOLAR DISORDER AND IT'S EMERGENT TREATMENT

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## Abstract:

Bipolar disorder, also known as manic-depressive illness. The mood changes involved in bipolar disorder range from one extreme to another. At one extreme the person may feel excessively happy and excited with a huge increase in energy and activity. The combination of essential vitamin supplements with the body's natural supply of lithium reduces depressive and manic symptoms of patients suffering from bipolar disorder. Dark Therapy”, in which complete darkness is used as a mood stabilizer in bipolar disorder. The main goals of adjunctive psychotherapy for bipolar disorder include the education of patients, and when possible, caregivers, about strategies for the management of stress, the identification and intervention of early signs of recurrence, and how to keep regular lifestyle. First-line treatments for bipolar disorder include For acute mania Lithium Valproate (either divalproex sodium or sodium valproate)First-generation antipsychotics. Bipolar disorder characterised by two types of relapse, mania (elation with disinhibited, overactive behaviour) and depression. Relapse rates of 50% at one year and 70% at five years.

**Keywords:** Bipolar disorder, Therapy, Mania, Depression, Mood Change

## Introduction:

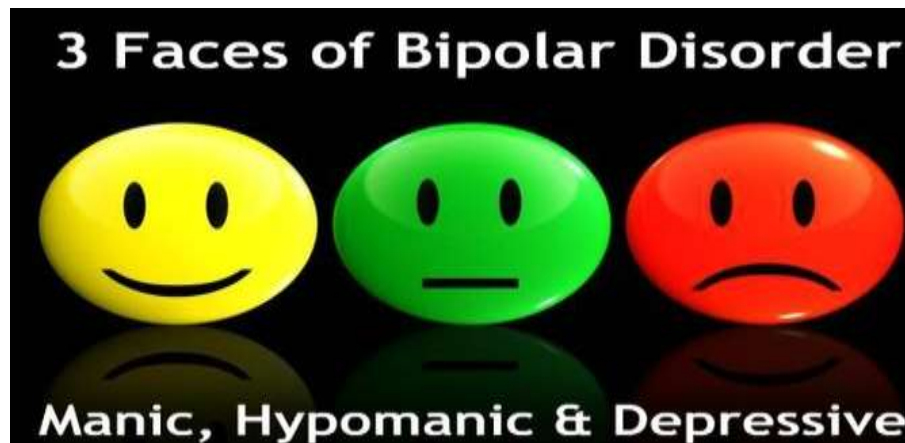
Generally our mood is appropriate for what is happening in our lives at the time. However, people who have bipolar disorder tend to have major changes in mood for no obvious reason. They may be extremely excited and happy when there is no reason to be. At other times they may feel very upset or sad even though lots of good things are happening in their lives. When a person has repeated mood swings which are very severe and which do not seem to occur for any good reason, it is likely that the person has a bipolar disorder. The mood changes involved in bipolar disorder range from one extreme to another. At one extreme the person may feel excessively happy and excited with a huge increase in energy and activity. This extreme mood swing is called ‘mania’ These mood swings usually last anywhere from a few weeks to a few months.<sup>1</sup> Bipolar disorder, also known as manic-depressive illness.<sup>2</sup>

It was previously referred to as manic depression, and bipolar affective disorder, or simply “bipolar.”<sup>3</sup> Bipolar I disorder by the occurrence of at least one manic or mixed episode. Unipolar mania is a rare disorder and is also conceptualised as part of the bipolar spectrum.<sup>(4)</sup>

At one extreme the person may feel excessively happy and excited with a huge increase in energy and activity. This extreme mood swing is called ‘mania’. At the other extreme the person may be severely depressed with a great loss of interest or energy. These mood swings usually last anywhere from a few weeks to a few months.<sup>1</sup>



**Fig. 1: Bipolar Phase**



**Fig 2: 3 Faces Of Bipolar Disorder**

Bipolar disorder arises from abnormalities within brain systems that modulate emotional behaviour, these various neuroimaging findings, have been relatively uncommon. Bipolar disorder most commonly begins in late adolescence and may include presyndromal affective, intentional, and behavioral disruptions prior to the first manic or depressive episode. bipolar disorder is progressive, in that euthymic periods between affective exacerbations steadily shorten.<sup>(5)</sup>

Bipolar disorder characterised by two types of relapse, mania (elation with disinhibited, overactive behaviour) and depression. Relapse rates of 50% at one year and 70% at five years. After a manic episode suggest the need for more effective therapeutic strategies to prevent relapses in bipolar disorder.<sup>(6)</sup>

#### **Historical Overview of Bipolar Disorder**

The high and low mood extremes seen in bipolar patients were first recorded in Greece during the first century and were described as distinct diseases. During the second century, a Greek physician identified these symptoms as part of a single disease.

From the second century for over a thousand years, Hippocrates' humoral hypothesis was the established theory of the cause for these mood extremes. Melancholia (depression) was due to a body fluid known as "black bile" and mania (insanity) was due to another body fluid called "yellow bile."

when a British physician referred to a disorder in which two mood extremes existed in a circular fashion within the same person, later to be known as "circular insanity" or "dual-form insanity."

In the nineteenth century Emil Kraepelin, a German psychiatrist considered to be the father of the modern concept of bipolar disorder, provided a clinical description in which he identified symptom-free intervals between the two extremes of mania and depression, and he coined the term *manic-depressive psychosis*.

Treatment for this mental illness was recorded by the Romans as early as the second century, when persons with symptoms of mania were described as being treated at lithium salt spas. It was believed the salts were absorbed by the body and provided a calming effect.

In the eighteenth century there was a change from religious authority to medical authority over people with mental illness. It was believed that insanity was caused by brain damage from outward influences.

eighteenth century, due to lack of success and overcrowding of hospitals, attitudes again changed, Those with mental illness were now considered "genetically inferior".

By the middle of the nineteenth century, medical psychiatry began to treat patients in small asylums, and by the end of that century, treatments consisted of high-pressure showers, sheep thyroid injections, metallic salts, horse serum, arsenic, tooth extractions, and insulin comas.<sup>2</sup>

#### **THE SEVERITY OF THE ILLNESS**

In bipolar disorder these mood swings may be so severe that they interfere with normal activities and everyday living. Mood swing may be so severe that they disrupt work and relationships. The severity of illness differs from one person to another. Some people may have frequent and severe episodes of mania and depression. Other people may only rarely become unwell. For each person the severity of illness differs from one episode of illness to another. Some episodes may be so severe that the person needs to spend time in hospital. However, other episodes could be very mild and may not need hospital care. With early treatment the episode of illness is likely to be less severe and hospital admission may be avoided. With early treatment the episode of illness likely to be less severe and hospital admission may be avoided.<sup>1</sup>

#### **Types of Bipolar Disorder**

There are several types of bipolar disorder differentiated by the varying symptoms individuals present with and the history of the person's experience.

**Bipolar I Disorder:** The individual who receives this diagnosis is experiencing a manic episode or has a history of one or more episodes. The person may or may not have experienced depressive episodes, and psychotic features or catatonia (stupor and either rigidity or extreme flexibility of the limbs) may be present.

**Bipolar II Disorder:** The individual given this diagnosis has had recurrent bouts of major depression with episodic hypomania. The person may present with or have a history of depression or hypomania but has never had a full manic episode. Psychotic or catatonic features may be evident.

**Cyclothymic Disorder:** This diagnosis is given to an individual who has had a chronic mood disturbance of at least two years' duration (one year in children) without symptom relief for longer than two months that includes many bouts of elevated mood that do not meet the criteria for hypomania. The person will have had many periods of depressed mood sufficiently severe or of a duration that meets the criteria for major depressive disorder.

**Substance/Medication-Induced Bipolar Disorder:** The mood disturbances characteristic of this disorder are considered to be the direct result of the physiologic effects of a substance of abuse or a medication. Symptoms can occur due to either intoxication or withdrawal.

**Bipolar Disorder Due to Another Medical Condition:** This disorder is characterized by symptoms of manic episodes considered to be due to the physiologic consequence of another medical condition and results in distress or impaired functioning. Such medical conditions include:

- oAIDS
- oBrain tumors
- oCushing syndrome
- oEncephalitis
- oHead injury
- oHuntington's chorea
- oHyperthyroidism or hypothyroidism
- oInfluenza
- oLyme disease
- oMultiple sclerosis
- oNeurosyphilis
- oStroke
- oSystemic lupus erythematosus
- oTemporal lobe seizures<sup>2</sup>

### **Etiology and pathophysiology**

The symptomatic structure of BD is predominantly depressive symptoms of varying severity. Atypical depressive symptoms (e.g., fatigue, hyperphagia) could possibly mediate sedentary inactive lifestyle and excess carbohydrate ingestion in BD.<sup>(7)</sup>

### **Heredity**

This disorder can be inherited and runs in families. These findings suggest that there is likely to be some kind of faulty gene in the body. If someone in the family has bipolar disorder, other family members are more likely to develop this disorder than people who do not have a relative with bipolar disorder.

### **Chemical disturbance**

People with this disorder seem to have a disturbance of the chemicals in the brain. It is likely that the faulty gene causes the body to produce the wrong balance of chemicals.

### **Personality factors**

The personality factors may influence the onset of this disorder. Many people who have probably inherited the faulty gene from their parents do not go on to develop bipolar disorder. It is possible that, among people who carry this gene, those who tend to have a moody personality and who do not handle stress very well may be more at risk of developing the disorder.

### **Stress**

Stressful life events (such as the loss of a loved one or childbirth) may increase the chance of developing bipolar disorder among those who are at risk. Stressful events such as these may also make further phases of mania and depression more likely among those who already have this disorder. Stress alone, however, does not seem to be enough to cause the disorder among people who have no other risk factors.<sup>1</sup>

### **Behavioral**

- Poor self-care
- Passive coping skills
- Depressive and negative symptoms
- Comorbid conditions, eg, tobacco and alcohol abuse;binge eating disorder
- Treatment noncompliance



**Biological**

- HPA axis hyperactivity
- Sympathetic nervous system hyperactivity
- GH suppression
- Gonadal hormone suppression
- Leptin inefficiency
- Obesity
- Medication

**Sociodemographic**

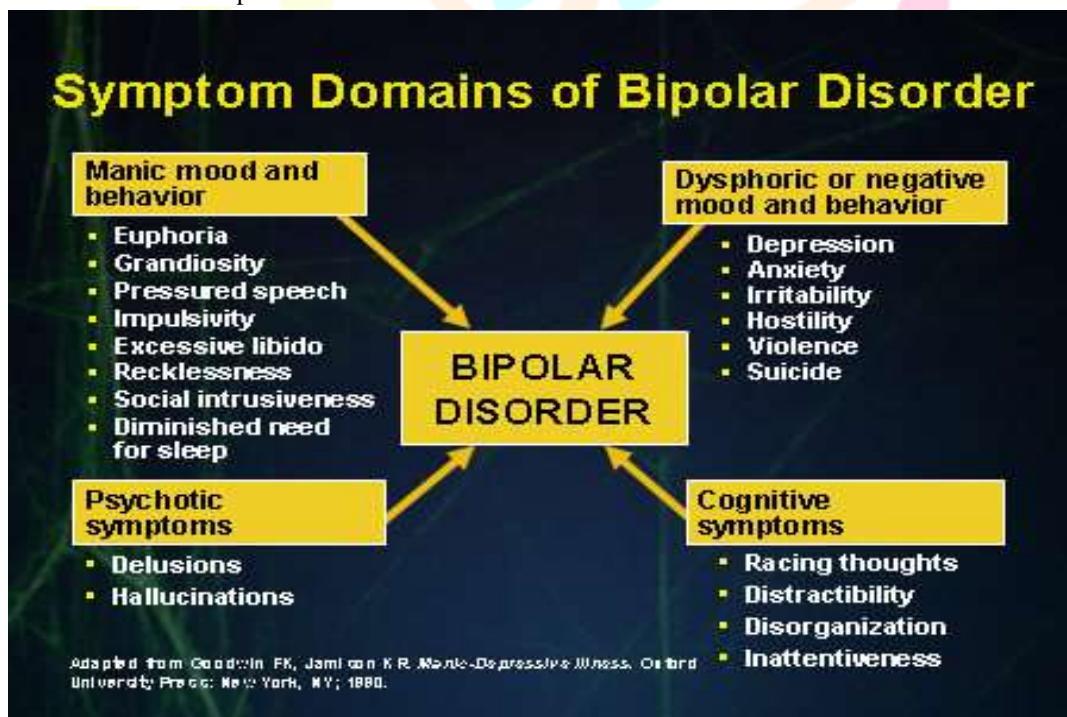
- Single
- Poor social support
- Unemployed
- Lower socioeconomic means
- Limited access to health care<sup>(7)</sup>

**Sign and symptoms**

Bipolar disorder afflicts 3 to 5% of the population with detrimental effect on life chances.<sup>(8)</sup>

Bipolar disorder shares symptoms of depression with unipolar depressive disorder, but is defined by episodes of mania or hypomania. Depression can include affective symptoms such as a pervasive sadness (depressed mood), a lack of pleasure or interest in activities (anhedonia/apathy), and irritability (in pediatric patients); cognitive symptoms such as decreased self-esteem and concentration, indecisiveness, feelings of guilt, and suicidal thoughts; and physical symptoms such as psychomotor retardation or agitation and either an increase or decrease in sleep, appetite, or energy.

In some ways the mirror image of depression, mania can include affective symptoms such as euphoric, expansive, or irritable mood; cognitive symptoms such as inflated self-esteem, distractibility, and racing thoughts; and behavioral symptoms such as increased psychomotor activity, increased goal-directed activity, and impulsivity. A distinctive (but not always present) symptom of mania is a decreased need for sleep.<sup>(9)</sup>



**Fig 3: Symptoms Of Bipolar Disorder**

**Diagnosis of Bipolar Disorder**

The diagnosis of bipolar disorder requires that a person has suffered one or more episodes of mania with or without episodes of depression at other times during the life history. This requirement for the occurrence of an episode of mania at some time during the course of illness distinguishes bipolar disorder from the more common form of mood disorder in the population, namely unipolar disorder (also commonly known as unipolar major depression or simply unipolar depression) in which subjects suffer one or more episodes of depression without ever experiencing episodes of pathologically raised mood.<sup>(10)</sup>

Some Diagnostic tests that doctors might conduct are:

- 1) **Physical exam:** May help identify any medical problems that could be causing one's symptoms.
- 2) **Psychological evaluation:** Mental health assesses one's thoughts, feelings and behavior patterns.
- 3) **Mood charting :** A record of moods, sleep patterns or other factors that could help with diagnosis.

### Risk factors

The following factors that have been suggested to be related to an emergence of BPD:

- 1) Demographic factors (gender, ethnicity).
- 2) Factors related to birth (pregnancy and birth complications, birth seasonality, urban birth, birth order).
- 3) Personal background (premorbid intelligence quotient, handedness, premorbid adjustment).
- 4) Social background (socioeconomic status of subjects and parents, recent stressful life events), family background (family dysfunction, parental loss).
- 5) History of medical conditions (childbirth, traumatic brain injuries, seizure disorders, multiple sclerosis).
- 6) Therapeutic including antidepressants, electroconvulsive therapy, acute tryptophan depletion and adverse effects of pharmacological agents; endocrine disorders; psychiatric comorbidity; and temperament and creativity [see the following review papers that predict the later first-ever onset of BPD].<sup>(11)</sup>

### Treatment of bipolar disorder<sup>12</sup>

#### Medication

#### Psychotherapy

#### Other Complementary

#### Medication Treatment

#### First-line treatments for bipolar disorder

First-line treatments for bipolar disorder include For acute mania Lithium Valproate (either divalproex sodium or sodium valproate) First-generation antipsychotics

Second generation antipsychotics Olanzapine Risperidone

Quetiapine

Zispridone

Aripiprazole

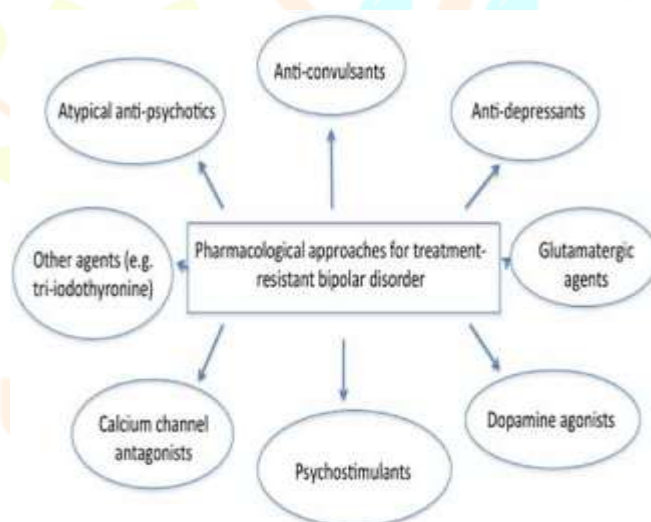


Fig. 3. Pharmacological treatment Of Bipolar Disorder

### Psychotherapy<sup>13</sup>

Psychological approaches build on evidence that psychosocial stressors, including excessive family discord or distress, negative life events, or events that disrupt sleep and wake rhythms or accelerate goal attainment are associated with relapses and worsening symptomatic states.

The main goals of adjunctive psychotherapy for bipolar disorder include the education of patients, and when possible, caregivers, about strategies for the management of stress, the identification and intervention of early signs of recurrence, and how to keep regular lifestyle (eg, sleep and exercise) habits. Moreover, in view of the high rate of non-adherence to drug treatments (up to 60% after acute episodes), psychosocial treatments emphasise consistency with pharmacotherapy.

### Other Complementary

**a) Cognitive-behavioural therapy** Cognitive-behavioural therapy presumes that recurrences of mood disorder are determined by pessimistic thinking in response to life events and core dysfunctional beliefs about the self, the world, and the future. Cognitive-behavioural therapy to treat depression has been adapted for patients with bipolar disorder with recognition that manic episodes are often associated with excessively optimistic thinking. One randomised controlled trial reported that patients who received 12–

14 sessions of cognitive-behavioural therapy were less likely to have depressive episodes and had better social functioning than patients in routine care for 30 months.

However, an effectiveness trial (n=252) comparing cognitive-behavioural therapy with treatment as usual in five UK community care centres found no advantage for cognitive-behavioural therapy over 18 months, except among patients with fewer than 12 previous episodes.

**b) Family-focused therapy** Family-focused therapy is based on the frequently replicated association between criticism and hostility in caregivers (so-called expressed emotion) and an increased likelihood of relapse in mood disorders and schizophrenia. Family-focused therapy involves the patient and caregivers (parents or spouse) in up to 21 sessions of psychoeducation, communication skills training, and problem-solving skills training.

Two randomised controlled trials including symptomatic patients with bipolar I and II found that, in the 1–2 years after a manic, mixed, or depressive episode, patients with bipolar disorder who received family-focused therapy and pharmacotherapy had 30–35% lower rates of relapse and rehospitalisation and less severe symptoms than did patients in case management or equally intensive individual treatment.

Two randomised controlled trials in paediatric populations—one in adolescents (aged 12–18 years) with bipolar disorder and one in children and adolescents (aged 9–17 years) with depression or hypomania with a first degree relative with bipolar disorder—found that children and adolescents who received family-focused therapy and pharmacotherapy recovered more rapidly from depressive episodes (HR 0.37–0.54) than did children and adolescents in brief psychoeducation and pharmacotherapy.

The education of caregivers about bipolar disorder might translate into benefits for patients, even if patients do not attend educational sessions. In one randomised controlled trial, remitted patients whose relatives attended psychoeducation groups had longer intervals before manic and hypomanic episodes than did those whose relatives did not attend groups.

In a second trial, patients whose caregivers attended 12–15 family education sessions showed significant decreases in symptoms of depression, especially if caregivers also showed mood improvement. Thus, adjunctive family interventions have the potential to lengthen periods of stability and alleviate residual symptoms in maintenance care. However, differences in treatment preferences, cultural factors (eg, willingness to disclose in front of others), and family structure (eg, parental vs spousal) might affect the willingness of patients or caregivers to participate in family-based treatment.<sup>13</sup>

**c) Light Therapy** Morning light appeared most effective for patients with unipolar depression; in contrast, patients with rapid cycling BD responded more favorably to midday light compared to morning or evening. The standard 10,000 lux, ultraviolet-blocked, white fluorescent light box presents minimal risk for adverse outcomes in most patients.

The efficacy and side effects of light therapy are affected by two important factors, the light dose and the time of day of light exposure. The dose is determined by the intensity emitted from the light source, distance from the light box, and duration of exposure. Most light sources provide 10,000 lux (illuminance at the receiving surface). Although recommendations for the treatment of seasonal affective disorder (SAD; major depressive disorder or BD with a seasonal pattern, according to the DSM-IV) suggest a starting dose of 10,000 lux of morning light for 30 min daily, there are no specific guidelines for the treatment of BD other than the need for anti-manic agent coverage.

Investigators have used 2,000 lux of morning light for 2 h daily, 400 lux for 2 h daily, and 10,000 lux for 45–60 min twice daily with reduction of depressive symptoms in patients with BD.

Side effects: Commonly reported side effects of light therapy include headache, eyestrain, agitation, and nausea. Patients with a BD I pattern of SAD are more likely to develop agitation with bright light compared to BD II or unipolar depressed patients.

Severely ill patients with BD have experienced light-induced worsening of depressive symptoms, ultrarapid cycling, mixed states and suicidality. New-onset suicidal ideation that required hospitalization occurred in three out of nine rapid cycling patients despite continuation of anti-manic drug treatment during light therapy with 10,000 lux light boxes.

The effects of different light spectra on mood indicated that red light is the least likely wavelength to cause changes in depressive symptoms. The colored wavelength range above 600 nm, which appears as red, has negligible effect on melatonin suppression, circadian rhythm phase shifting, and clinical response in patients with SAD.

Bright light therapy is a potentially valuable modality for patients with bipolar depression (whether seasonal or non-seasonal) because:

- The light dose can be titrated on a daily basis against emergent side effects and hypomania.
- major side effects are rare.
- drug–drug interactions are avoided in a group of patients likely to be taking multiple medications.
- The treatment is affordable and readily disseminated.<sup>(14)</sup>



Fig. 4: Family Focused Therapy

#### d) Dark therapy for bipolar disorder using amber lenses for blue light blockade

Dark Therapy”, in which complete darkness is used as a mood stabilizer in bipolar disorder. darkness itself appears to organize and stabilize circadian rhythms. complete darkness from 6 p.m. to 8 a.m. the following morning.

On the physiology of human circadian rhythm suggests that “virtual darkness” may be achievable by blocking blue wavelengths of light. A recently discovered retinal photoreceptor, whose fibers connect only to the biological clock region of the hypothalamus, has been shown to respond only to a narrow band of wavelengths around 450 nm. Amber-tinted safety glasses, which block transmission of these wavelengths, have already been shown to preserve normal nocturnal melatonin levels in a light environment which otherwise completely suppresses melatonin production.

Therefore it may be possible to influence human circadian rhythms by using these lenses at night to blunt the impact of electrical light, particularly the blue light of ubiquitous television screens, by creating a “virtual darkness”. One way to investigate this would be to provide the lenses to patients with severe sleep disturbance of probable circadian origin.<sup>(15)</sup>

#### e) Mindfulness-based Cognitive Therapy (MBCT) in bipolar disorder

(Mindfulness-based Cognitive Therapy: MBCT) for people with bipolar disorder focusing on between-episode anxiety and depressive symptoms.

MBCT teaches people skills that enable them to become more aware of their thoughts without judgment, viewing negative (positive and neutral) thoughts as passing mental events rather than as facts. MBCT has proven effective in preventing relapse in recurrent depression. The treatment is closely based on an approach that is known to be helpful in the treatment of anxiety disorders (Mindfulness-based Stress Reduction , so this study provides an opportunity to evaluate its impact on between-episode anxiety in bipolar patients .risk factors include depression and anxiety comorbidity.<sup>(16)</sup>

**f) Acupuncture** The development of various classes of antidepressant drugs, represented by selective serotonin reuptake inhibitors (SSRIs), has considerably improved the prognosis and the tolerability in the treatment of depressive disorders, the currently available antidepressant therapy is unsatisfactory.

There remains a large portion of depressed patients who cannot obtain full responses and experienced recurrent episodes. Undesirable side effects and delay in the onset of the therapeutic action also have hampered the clinical use of antidepressant medications . In order to overcome these shortcomings, strenuous attempts have been made to search for alternative strategies that could improve the outcomes of antidepressant treatments. As an ancient therapeutic modality, acupuncture therapy has become a widely recognized alternative therapy in today clinical practice. As a result, numerous clinical studies aimed at evaluating the efficacy and safety of acupuncture in patients with depressive disorders have been reported over the past decades, especially for major depressive disorder (MDD) and post-stroke depression.<sup>(17)</sup>



Fig. 5: Acupuncture Therapy

**g) Nutritional therapy** Taurine is an amino acid made in the liver from cysteine that is known to play a role in the brain by eliciting a calming effect. A deficiency of this amino acid may increase a bipolar patient's manic episodes. In addition, eighty percent of bipolar sufferers have some vitamin B deficiencies (often accompanied by anemia).The combination of essential vitamin supplements with the body's natural supply of lithium reduces depressive and manic symptoms of patients suffering from bipolar disorder.



Depression has for some time now been known to be associated with deficiencies in neurotransmitters such as serotonin, dopamine, noradrenaline, and GABA. As reported in several studies, the amino acids tryptophan, tyrosine, phenylalanine, and methionine are often helpful in treating many mood disorders, including depression. Tryptophan is a precursor to serotonin and is usually converted to serotonin when taken alone on an empty stomach. Therefore, tryptophan can induce sleep and tranquility and in cases of serotonin deficiencies, restore serotonin levels leading to diminished depression.<sup>(18)</sup>

#### h) Natural therapy

Bipolar patients with predominantly depressive symptoms often respond well to pranayama and asanas. Ujjayi breathing is safe and beneficial for most bipolar patients because it is calming as opposed to stimulating.<sup>(19)</sup>

#### Suicidal Behaviour in Bipolar Disorder

Bipolar (manic-depressive) disorder is a common and severe illness. It is also potentially fatal as a result of accidents and increased mortality associated with comorbid substance use and medical illnesses, but its highest lethality results from suicide. Suicide rates, averaging 0.4% per year in men and women diagnosed with bipolar disorder, are >20-fold higher than in the general population. Suicidal acts often occur early in the illness course and in association with severe depressive and dysphoric-agitated mixed phases of illness, especially following repeated, severe depressions.<sup>(20)</sup>

#### Reference:

- Pearson V, Devon NH, Council DC. Homelessness Health Needs Assessment.
- By Judith Swan, MSN, BSN, AND, RN; Persis Mary Hamilton, EdD, MSN, BSN, RN,PHN,PMHN Depressive Disorders COPYRIGHTS 2017, WILD IRIS MEDICAL EDUCATION, INC ALL RIGHTS RESERVED
- [www.learninpharmacy.ie](http://www.learninpharmacy.ie),
- Heinz Grunze The Treatment of mania practical management of Bipolar Disorder, eda. Allan H. Young I. Nicol Ferrier and Erin E. Michalak Published by Cambridge University Press; 2010; 1-199
- Stephen M. Strakowski, Caleb M. Alder,(...), and Jennifer D. Townsend , The functional neuroanatomy of bipolar disorder: a consensus, An International Journal of Psychiatry and Neurosciences; 2012, 14, 313-325
- Alison Perry, Nicholas Tarrier, Richard Morriss, Eilis McCarthy, Kate Limb, Randomised controlled trial of efficacy of teaching patients with bipolar disorder to identify early symptoms of relapse and obtain treatment, BMJ 1999, 318, 149-153
- Rogers s. Mcintyre, MD, FRCPC, Jakub z. Konarski, MSc, PhD, candidate, virginia L. Misener, PhD, Sidney H. Kennedy, MD, FRCPC, Bipolar Disorder and Diabetes Mellitus: Epidemiology, Etiology, and Treatment Implications Annals of clinical psychiatry; 2005, 17(2): 83-93
- Robert L. Leahy, Bipolar Disorder: Causes, Contexts , and Treatments Wiley Interscience; 2007, 63(5), 417-424
- Terence A. Ketter, MD Diagnostic Features, Prevalence, and Impact of bipolar disorder Psychlopedia; 2009
- Nick Craddock, Ian Jones Genetics of bipolar disorder journal of medical genetics; 1999, 36(8), 585-594
- Kenji J Tsuchiya, Majella Byrne and Preben B. Mortensen, Risk factors in relation to an emergence of bipolar disorder : a systematic review Bipolar Disorders; 2003, 5, 231-242
- M. Glitin Geffen School of Medicine At UCLA, Los Angeles, CA, USA Treatment-resistant bipolar disorder Molecular Psychiatry (2006) 11, 227-228
- John R. Geddes and David J. Miklowitz , Treatment of bipolar disorder HHS Public Access; 2013, 381(9878), 1672-1682
- Dorothy Sit, Katherine L. Wisner, Barbara H. Hanusa, Stacy Stull and Michael Terman, Light therapy for bipolar disorder: a case series in women Bipolar Disorders ; 2007, 9, 918-927
- James Phelps, Dark therapy for bipolar disorder using amber lenses for blue light blockade medical hypothesis; 2008, 70(2), 224-229
- J.M.G. Williams, Y. Alatiq, C. Crane, T. Barnhofer, M. J. V. Fennel, D. S. Duggan, S. Hepburn G.M. Goodwin, Mindfulness-based Cognitive Therapy (MBCT) in bipolar disorder : Preliminary evaluation of immediate effects on between-episode functioning Journal of Affective Disorders; 2008, 107, 275-279
- Zhang-Jin Zhang, Hai-Yong Chen, Ka-chee Yip, Roger Ng, Vivian Taam Wong, The effectiveness and Safety of acupuncture therapy in depressive disorder: systematic review and meta-analysis Journal of Affective Disorders; 2009, 1-13
- Shaheen E. Lakhan and Karen F. Vieira Nutritional therapies for mental disorders nutritional Journal; 2008, 7(2)
- Richard p. Brown, M.D., and Patricia L. Gerbarg, M.D. Sudarshan Kriya Yogic Breathing in the treatment of stress, Anxiety, and depression; Part II- clinical Application and Guidelines The Journal of Alternative and Complementary Medicine; 2005, 11(4), 2005, 711-717
- Leonardo Tondo, Goran Isacson, Ross J. Baldessarini Suicidal behaviour in bipolar disorder CNS Drugs; 2003, 17(7), 491-511