# Bipolar Mood Disorder

Bipolar is a mental condition characterized by episodes of mania (or hypomania) and depression. Patients with this condition experience emotional highs and lows causing mood swings. The alternating episodes of mania and depression are caused by the varying levels of serotonin, norepinephrine, and dopamine main neurotransmitters in the brain. Therefore, management of this condition targets correcting the levels of the three neurotransmitters in the patient. The treatments focus on eliminating the depression or maniac symptoms without causing the extreme reverse. Since this cannot often be achieved using one drug, the patient often is put on more than two drugs to manage this condition effectively. This paper explains the pathophysiology of bipolar disease, theories on the development of the condition and its treatment modalities.

## Epidemiology, Causes, Course Signs and Symptoms of Bipolar Disease

Bipolar affects 1% of the world population and over 3% of the US population. The condition has a median onset age of 25 years (Singh & Dean, 2017). In the US, 2.65% of the population less than 18 years are living with this condition. Whereas the condition is common in both sexes, women have a higher chance of experiencing rapid cycling as compared to their male counterparts in a threefold (Singh & Dean, 2017). Besides, women with this condition experience prolonged depression and mixed episodes compared to males. World health organization ranks bipolar disorder as the sixth common cause of disability. Besides, it is approximated that the condition reduces the life expectancy of the by 9-10 years because one in every five people with this condition commit suicide.

Bipolar is caused by a combination of factors including genetical and environmental factors. Whereas the condition is idiopathic, many factors can be attributed to causes. These include prolonged stress and history of child abuse (Singh & Dean, 2017). Other conditions factors include drug use and other mental illness, but their mechanism of causation is poorly understood. Environmental factors may include low self-esteem, financial emotional and physical stress (Katzung & Trevor, 2015). Finally, genetics play a significant role in the transmission of the disease. It is approximated that two-thirds of children whose parents or families have this condition develop the condition.

Symptoms of bipolar disorder depend on the phase of the condition. During the mania or hypomania phase, patients experience symptoms explained as highs. For example, they feel elated or very up often caused by an alteration in epinephrine levels and dopamine (Singh & Dean, 2017). Besides, the patients feel high levels of energy which may make them violent. The patients also increase the levels of activity making them very active and can be described as wired or jumpy. As such, patients with mania phase experience difficulties in sleep. Maniac patient experience disorders of thought like pressured speech and verbal diarrhea (Singh & Dean, 2017). Besides, during the manic phase, the sex drive is high, and patients may turn to reckless sex. Their spending habits change with patients becoming extravagant endeavors and other risky behaviors (Ashok et al., 2017). Finally, agitation in mania phase is very common; the patients get irritable and touchy which increases their chances of becoming violent.

In the depressive phase, patients are often down, sad and empty with signs of hopelessness. The patients show low energies making them lonely and not interested in activities (Koller & Edenberg, 2014). In some patients, they may lack sleep feeling boredom and not able to enjoy anything. For learners, there are troubles in concentration and have a higher difficulty to remember since they pay low attention (Grunze, 2015). Some patients may have suicidal ideation thus need close monitoring. The appetite of the patients in depression varies in extremes of excess appetite or very low making patient to the consumer either very little or too much food.

Depending on the nature of the symptoms, bipolar disorder can be classified into various categories. For example, patients experiencing maniac episodes for more than seven days have the bipolar I disorder (Grunze, 2015). These patients need acute care in a hospital setup as they are a danger to themselves and others. Whereas depressive episodes can occur in bipolar I disorder, they typically last for two weeks and are rare. Patients exhibiting depressive episodes and hypomania for more than one week have bipolar II disorder. Unlike bipolar I, these patients lack full-blown manic episodes (Ashok et al., 2017). In some instances, patients may have periodic episodes of hypomania and depression may last for two years and reappear later. These patients are considered to have cyclothymic or cyclothymia. Finally, some episodes of bipolar disorder do not match any of the criteria thus are unclassified. Classification of the disorder makes it easy to manage through identification of periods of hospitalization and community care (Katzung & Trevor, 2015). Whereas the maniac and depressive phases of bipolar normally occur in isolation some patients may experience mixed symptoms of mania and depression.

Bipolar is a chronic condition with mania and depression recurring over the lifespan. However, patients experience normalcy in between the episodes leading a normal life with 33% of the population experiencing residual symptoms (Ashok et al., 2017). In some people, the symptoms may be permanent despite the treatment (Singh & Dean, 2017). Such people will experience longtime chronic conditions that do not remit even when treated. People with this condition can lead a normal life if they continue taking medications. However, when patients are not treated or undertreated the condition will tend to worsen (Ashok et al., 2017). Prolonged periods without medications often leads to more often and rapid cycling episodes of depression and mania than the initial symptoms. Besides, suicidal ideation increase and patients may make many attempts (Singh & Dean, 2017). In the manic phases, such people are a danger to themselves due to the risk of suicide and others due to ease of irritability and the high energy levels. Patients with treatment lead a normal life with few episodes in their lifetime.

## Predominant Biological Theory of Bipolar Disease

The predominant theory on the pathogenesis of bipolar disorder is primarily on monoamines. The maniac and depressive symptoms have been attributed to the dysregulation of monoamine neurotransmitters in the brain (Grunze, 2015). The theories include the cholinergic aminergic balance theory, permissive hypothesis of serotonin and the dopamine theory of bipolar disorder. The cholinergic aminergic balance theory articulates the mania episodes to the decreased cholinergic signaling with an increase in adrenergic (Ashok et al., 2017). On the other hand, the permissive hypothesis postulates on the ability of serotonin imbalance to cause both mania and depression (Ashok et al., 2017). However, the predominant theory in the biological basis of bipolar disorder is the dopamine hypothesis of bipolar disorder.

## The Dopaminergic Theory of Bipolar Disease

The dopaminergic theory was proposed in the 1970s to explain the molecular basis of bipolar disorder (Ashok et al., 2017). Initially, the theory was established to show the occurrence of mania especially to patients who took amphetamines. The theory was used to justify the fact that dopaminergic drugs were anti-maniac. However, later the theory was incorporated to explain both the depressive and manic symptoms in bipolar (Ashok et al., 2017). It was noted that while the use of dopaminergic drugs treated mania resulting from amphetamine use, patients often developed depression. The use of dopaminergic drugs is associated with hypodopaminergia while the use of amphetamines causes hyperdopaminergic. Therefore, the dopaminergic theory of bipolar disorder postulates that if the depressive phase of BD is associated with hypodopaminergia, then the mania phase of BD is associated with hyperdopaminargia (Ashok et al., 2017). Therefore, depression and mania in bipolar disease are caused by opposing the influence of the different concentration of the monoamines neurotransmitters in the brain that regulates affect.

The theory proposes that alterations in the normal homeostasis of the functions of dopaminergic transmitters cause recurring changes in neurotransmitters. For instance, a homeostasis mechanism triggered to correct hypodopaminergia leads to hyperdopaminargia which shows the patient transit from depression symptoms to mania (Ashok et al., 2017). Borrowing from this, the theory proposes that the symptoms of both mania and depression are caused by faulty homeostatic overregulation of the dopaminergic neurotransmitters in the brain. For instance, faulty dopaminergic homeostasis in a depressed patient with hypodopaminergia well-read to a rapid increase in dopaminergic neurotransmitters causing mania. Similarly, defective homeostasis in patients with mania will lead to over-reduction of dopaminergic function leading to depression due to hypodopaminergia (Ashok et al., 2017). The aim of treatment by this model is to correct the erratic homeostasis leading to normalization. When the patients with BD achieve normal homeostasis in the dopaminergic function, euthymic and remission ensures.

## Molecular Physiology of Bipolar Disease

Alteration in three neurotransmitters has been caused bipolar disease. These are biogenic amines namely norepinephrine, dopamine and serotonin. The neurotransmitters through the effect on various receptors in the brain mediate the symptoms of bipolar like stress, mood, pleasure sleep attention concentration and arousal among other higher brain cognitive functions (Ashok et al., 2017). In their normal concentration, the neurotransmitters are regulated to give a person a normal behavior but the dysregulation results mania, depression or both (Ashok et al., 2017). Achieving normalcy in bipolar patient needs administration of agents that will restore the balance of the three neurotransmitters through interaction with their receptors in the brain. However, administration of these extrinsic agents may have an additional unwanted effect since the majority of neurotransmitters have receptors in other parts of the body.

Dopamine is a reward center neurotransmitter synthesized from amino acid tyrosine. It is a catecholamine synthesized both in the kidney and brain and is a precursor to L-dopa. Dopamine is secreted in the brain neurons and other body parts where it binds to five Dopa receptor (D1, D2, D3, D4, and D5) (Ashok et al., 2017). Whereas the receptors are primarily found in the brain, some types are found in the cardiovascular system and renal system. In the brain, dopamine controls both higher and lower cognitive functions. Higher cognitive functions include motivation, reward and motor control among others. The lower levels functions of dopamine include regulating sleep, sexual arousal, and lactation (Koller & Edenberg, 2014). Various drugs can affect the action of neurotransmitter dopamine due to their actions on dopamine receptors. Bromocriptine, for example, binds to dopamine two receptors to decrease lactation. Other drugs that potentiate the action of Dopamine include cocaine, Apomorphine, and amphetamines (Singh & Dean, 2017). On the other hand, Metoclopramide, some neuroleptics and domperidone antagonize the action of dopamine (Katzung & Trevor, 2015). Dopamine has a role in bipolar since the levels are high during the manic episodes and low during depressive episodes.

The neurotransmitter Norepinephrine, on the other hand, is synthesized from dopamine. Norepinephrine is both a hormone and neurotransmitter. Once secreted the transmitter can bind to alpha (1and 2) and beta (1 and 2) receptors to cause their action. Norepinephrine prepares the body for response to stress, anxiety, restlessness, promotes vigilance, increases alertness, memory retrieval, and attention (Koller & Edenberg, 2014). In the cardiovascular system, it increases blood pressure and heart rate as well as glycogenesis (Grunze, 2015). Drugs enhance the actions of norepinephrine like clonidine, sympathomimetic, and isoprenaline and inhibited by drugs like antipsychotics, antidepressants, and beta blockers. The levels of norepinephrine are high in mania and low in depression. The amino acid tryptophan is the precursor of serotonin. Like the other neurotransmitters, serotonin is a neurotransmitter in the brain with receptors in the body. Serotonin binds to 5HT1-5HT7 receptors causing various actions (Katzung & Trevor, 2015). The higher cognitive functions include regulation of stress, mood, happiness, and reduction of depression. Lower level functions of serotonin include stimulation of nausea and control of sleep. The actions of serotonin are potentiated by Monoamine oxidase inhibitors (MAOIs) and selective serotonin inhibitors (SSRIs)

## Treatment of Bipolar Disease

Treatment of bipolar disorder aims at eliminating the manic and depressive symptoms through the restoration of neurotransmitter balance in the brain. Three classes of medications are commonly prescribed for bipolar are antipsychotics, mood stabilizers, and antidepressants.

Antipsychotics are effective in the short-term prevention of mania symptoms like delusions and hallucinations. Majority of the antipsychotics are inhibitors of dopamine receptors D2 and serotonin (5HT receptors). The mainly used antipsychotics in bipolar are olanzapine risperidone, Quetiapine, and clozapine. Olanzapine and clozapine eliminate depressive episodes by inhibiting competing with serotonin by binding to most 5HT receptors (Katzung & Trevor, 2015). Risperidone binds to D2 receptors in the mesolimbic pathway reducing dopaminergic transmission. Risperidone is more selective to dopamine receptors than serotonin. Both drugs are taken orally and are readily absorbed in the small intestines as they have a high lipid binding capacity (Katzung & Trevor, 2015). They are metabolized in the life to both active and inactive metabolites and created by the kidney with a half-life of 12 hours. The inhibition of dopamine and serotonin receptors caused by these drugs caused various side effects. For instance, they can cause constipation, mouth dryness and difficulty in ANS through blockage of muscarinic receptors (Katzung & Trevor, 2015). Besides, these drugs can cause supersensitivity to dopamine receptors causing tardive dyskinesia. In the endocrine system, they can cause lowered sex drive, infertility, and amenorrhea galactorrhea through blockage of dopamine receptors (Katzung & Trevor, 2015). Risperidone interacts with beta blockers to increase hypotension while clozapine interacts with benzodiazepines to increase sedation. Respiridone is contraindicated in angioedema and hypersensitivity (Katzung & Trevor, 2015). Olanzapine and clozapine are contraindicated in patients with dementia and hyperglycemia since it worsens these conditions.

Mood stabilizers reduce mania, depression or mixed symptoms by restoring dopaminergic homeostasis. They regulate the levels of monoamines (serotonin, dopamine and restoring the balance needed for the patient to attain normalcy. Lithium, Carbamazepine, Divalproex, Lamotrigine and valproic acid are examples of mood stabilizer (Katzung & Trevor, 2015). Carbamazepine inhibits the reuptake and releasing of serotonin through blocking brain voltage-gated sodium channels. Lithium prevents the production of dopamine and norepinephrine in the brain, potentiates the production of serotonin and agonizes its action. The decrease of dopamine and norepinephrine and increased of serotonin leads to stabilization of mood without causing opposite polarity. Lamotrigine binds to 5-HT type 1 to 7 receptors agonizing the action of serotonin (Katzung & Trevor, 2015). Lithium is excreted both in faces and urine un-metabolized and has a half-life of 24hours. Carbamazepine induces its metabolism and those of other drugs in the liver together with valproic acid and lamotrigine and is excreted in the kidney. Yohimbine, Quetiapine, and haloperidol agonize the actions of mood stabilizers (Katzung & Trevor, 2015). The drugs also interact with metoclopramide to cause nausea. Carbamazepine can cause ataxia and double vision due to the blockage of dopaminergic receptors and its action on blockage of voltage-gated sodium ion channels

Finally, in the depressive phase of bipolar disorder antidepressants can be used to elevate the mood of the patients. However, patient management is crucial when using antidepressants as they may precipitate mania. The commonly used antidepressants to manage to include Quetiapine, fluoxetine, and Lurasidone. Fluoxetine antagonizes the activity of serotonin through competitively binding to 5HT receptors in the brain thus elevating mood of the patient (Katzung & Trevor, 2015). Quetiapine binds specifically to 5HT2 in the brains and prevent serotonin from binding causing an increased level of happiness and relieves stress. Many of the antidepressants are taken orally with a high absorption rate and bind highly with lipids in the blood. Fluoxetine has a half-life of one day while Quetiapine has a half-life of 6 hours. Fluoxetine is metabolized in the liver to active metabolite norfluoxetine and excreted in the kidney while Quetiapine Fumarate is inactivated in the liver then excreted in urine (Katzung & Trevor, 2015). The action of various antidepressants on 5HT receptors causes increased appetite, sex drive, breast discharge and dry mouth (Katzung & Trevor, 2015). The drug Artane is used to counter the side effect of antidepressants and other antipsychotic. For this reason, it is used to treat the side effects of fluoxetine.

## Benefits, Risks and Ethical Consideration for Higher Risk and Exceptional Treatment of Bipolar Disease

Higher risk and exceptional treatments apply to patients without remission, children, and pregnant mothers. The treatments may include the prescription of experimental drugs or an altered disease to ensure their wellbeing. The primary benefit of is ensuring remission from bipolar and promoting wellbeing (Ashok et al., 2017). In children, treatments will promote learning and eliminate depression. Treatment of bipolar has many risks. For instance, treating children with depression with antidepressants increases their risk for suicide (Koller & Edenberg, 2014). Besides, use of antipsychotics poses a danger for diabetes or hyperglycemia. Furthermore, the drugs prescribed to pregnant mothers may endanger the lives of the children they carry (Singh & Dean, 2017). Prescription of higher risk and exceptional treatments needs an accurate diagnosis. For instance, a comprehensive diagnosis needs to be made to avoid giving a patient unnecessary treatment. Besides, honesty on the benefits and risks is crucial to minimize the harm to recipients (Katzung & Trevor, 2015). Combining non-pharmacological and counseling may contribute to quick remission thus should be considered.

## Conclusion

In conclusion, the chronic nature of bipolar mood disease needs long-term medication. The dopaminergic hypothesis of bipolar disease postulates that the condition occurs due to an imbalance in dopaminergic neurotransmitter. The main advantage this of this theory is that it accounts for both mania and depression while the theory is disadvantaged as it does not account for some current treatments for the condition. Whereas the patients benefit from remission, many side effects result from such treatments necessitating the need for accurate prescription and monitoring for the said side effects. The ethical consideration should focus on explaining the available approaches and respecting the rights of the individuals. The caregivers also should strive to manage the side effects as they may present to identify side effects and prevent them. Future studies should focus on finding on more safe medications for both children and adults.

## References

Ashok, A. H., Marques, T. R., Jauhar, S., Nour, M. M., Goodwin, G. M., Young, A. H., & Howes, O. D. (2017). The dopamine hypothesis of bipolar affective disorder: The state of the art and implications for treatment. *Molecular Psychiatry*, *22*(5), 666–679.

Grunze, H. (2015). Bipolar disorder. In *Neurobiology of brain disorders* (pp. 655–673). Elsevier.

Katzung, B., & Trevor, A. (2015). *Basic and clinical pharmacology.* McGraw-Hill Education.

Koller, D. L., & Edenberg, H. J. (2014). Identification of pathways for bipolar disorder: A meta-analysis. *JAMA Psychiatry*, *71*(6), 657–664.

Singh, A., & Dean, O. M. (2017). Beyond the therapeutic shackles of the monoamines: New mechanisms in bipolar disorder biology. *Progress in Neuro-Psychopharmacology and Biological Psychiatry*, *72*, 73–86.