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Review article

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Bipolar disorder, symptoms and its marketed drugs-a review

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ABSTRACT

Bipolar disorder is an illness of the brain that causes severe cycles in a person's frame of mind (mood), energy level, thinking and activities. According to the criteria defined in Diagnostic and statistical manual DSM-IV-TR, people with Type I bipolar disorder will experience at least one episode of mania that may include mixed, depressive and hypomanic episode. Similarly for type II bipolar disorder patients may experience only hypomanic and depressive episodes. But for Cyclothymic disorder they may be diagnosed by having not experiencing any manic, mixed and depressive episodes. They only experience numerous periods of both depressive and hypomanic symptoms for minimum of 2 year or with symptom free period. [3]

There are 4 types of bipolar disorders, bipolar I, II, cyclothymia, and bipolar disorder not specified. There is no single known cause for bipolar disorder as many provoking factors act together to produce the bipolar disorder illness. The symptoms that are seen in bipolar disorder are remarkable and erratic mood changes. The illness may have two strongly contrasting phases: mania and depression.

Keywords: Bipolar disorder, Diagnostic and statistical manual, Cyclothymic.

INTRODUCTION

Synonyms

Bipolar affective disorder, bipolar illness, manic depression, bipolar disease [1] [4] Bipolar disorder is an illness of the brain that causes severe cycles in a person's frame of mind (mood), energy level, thinking and activities. The disorder was first described by French scientist Jules Baillarger in 1854 as "dual-form mental illness." The term Manic-depression was coined by Emil Kraepelin. Later in 1980s, Manic depressive illness was replaced by Bipolar disorder as the name was used by psychiatrists to describe this condition [4].

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Bipolar disorder

[4]Bipolar disorder is considered as a brain disorder that causes severe shifts in mood, energy level, thinking, and behavior aspects.

For example, people with bipolar disorder may often experience episodes of overly high “highs”, extreme irritability, and depression conditions. While everyone has good and bad moods and can feel irritable, the unprovoked and intense highs and lows of people with bipolar disorder can be unpredictable, extreme, and debilitating. Patients with bipolar disorder can show four forms of mood

swings which includes: mania, depression, mixed episodes, and hypomania.

Bipolar disorder occurs in all age groups, young and old. Until recently, bipolar disorder in children and adolescents was thought to be an extremely rare condition, but it may, in fact, be more common than previously thought. However, not all children who have severe temper tantrums or moments of excessive moodiness, irritability, and overexcitement have bipolar disorder. For those with bipolar disorder, the mood cycles are prolonged, severe, and interfere with daily functioning.[4]

Different types of bipolar disorder [6]

Bipolar I disorder	—————→	Manic or mixed episode with or without psychosis and/or major depression
Bipolar II disorder	—————→	Hypomanic episode with major depression; no history of manic or mixed episode*
Cyclothymia	—————→	Hypomanic and depressive symptoms that do not meet criteria for bipolar II disorder; no major depressive episodes
Bipolar disorder not otherwise specified	—————→	Does not meet criteria for major depression, bipolar I disorder, bipolar II disorder, or cyclothymia (e.g., less than one week of manic symptoms without psychosis or hospitalization) [6]

Causes of bipolar disorder [4]

There is no single known cause for bipolar disorder as many provoking factors act together to produce the bipolar disorder illness. Most recent research points out that the leading contributor of bipolar disorder is through the inherited from their parents.

For example, evidence clearly shows that bipolar disorder mostly occurs in families having their parents with bipolar disorder leading to 4 to 6 fold of increased risk of developing the illness. This means that approximately 10 percent (1 in 10) of people who have a parent with bipolar I disorder will develop the illness themselves. The risk is even higher when full bipolar spectrum is considered. Scientists are currently working to identify which genes or the combinations of genes that are influencing the risk for bipolar disorder. However, genes are not the only factor that cause bipolar disorder but the studies of identical twins (those

who share the same genes) shows that other factors are also involved. If bipolar disorder was exclusively caused by genes then an identical twin of someone with bipolar disorder would always have to experience the illness themselves. Research shows this is not the case. Other biological, social, and emotional factors also must play a role in the development of the disorder. For example, clinical experience suggests that trauma or stressful life events can sometimes trigger an episode of bipolar disorder in people who are genetically vulnerable. In fact new research has found that stress hormones may change the way genes function, allowing illnesses like bipolar disorder to emerge [4].

Suspicion of bipolar disorder:

- A family history of people experiencing bipolar disorder or manic depression.
- Problems with alcohol consumption.

- A history of complicated and disrupted circumstances Eg. Includes multiple relationships, switching jobs frequently or frequent change of address.

Symptoms of bipolar disorder in children and adults [4]

The symptoms that are seen in bipolar disorder are remarkable and erratic mood changes. The illness may have two strongly contrasting phases: mania and depression.

SYMPTOMS DURING MANIC EPISODES

Mood:

- Elevated or overjoyed mood without a clear cause.
- Short-tempered, angry, or uncontrolled mood that is out of proportion to any reasonable cause.
- Sad or empty moods.
- Feelings of hopelessness or pessimism.
- Feelings of guilt, worthlessness, or helplessness.
- Lack of interest or delight in activities once enjoyed.
- Physical injury that is not responsible for causing pains.
- Irritability.

Thinking

- Having many thoughts at a time.
 - Thoughts that change from one idea to another without any correct judgement.
 - Distractibility or inability to concentrate.
 - Unrealistic and unshakable beliefs in one's abilities and powers.
 - Thoughts of suicide or death or a suicide attempt.
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- A depressive episode is diagnosed if a person has a depressed mood or loss of interest or pleasure along with a number of the symptoms listed above that last most of the day, nearly every day, for two weeks or longer. In children and adolescents, the mood may be irritable rather than sad.

- Difficulty concentrating, remembering, and making decisions.

Energy

- Prominent energy.
- Decreased need of sleep.
- Increased activity level.
- Decreased energy or a feeling of fatigue or of being "slowed down."

Behavior

- Increased activity level that coincides with changes in mood, thought, or energy.
- Speech that is faster, louder than usual, more difficult to interrupt.
- Flight of ideas.
- Giddy, silly, goofy behavior that cannot be stopped despite negative consequences.
- Angry behavior that results in destroyed property, physical aggression & crying.
- Inappropriate sexual behavior.
- Poor judgment.
- Restlessness or irritability.
- Sleeping too much or not enough
- Unintended weight loss or gain
- Social isolation.

ACCORDING TO THE DIAGNOSTIC AND STATISTICAL MANUAL OF MENTAL DISORDERS (DSM-IV-TR)

A manic episode is diagnosed if a person suffers from multiple diagnostic symptoms that last seven days or that require hospitalization. One of the mood symptoms must be irritability or elation to be diagnosed with mania. Also, these symptoms cannot be explained by other medical,

Neurologic, or mental health conditions and must impair or change the child's normal functioning.

- Children and adults with bipolar disorder frequently shows depression along with physical problems such as headache, stomach pain and feeling of tired. [4]

Symptoms in depressive episode may [7]

- ✓ Feel very down or sad.

- ✓ Sleep too much or too little.
- ✓ Feel like they can't enjoy anything.
- ✓ Feel worried and empty.
- ✓ Have trouble concentrating.
- ✓ Forget things a lot.
- ✓ Eat too much or too little.
- ✓ Feel tired or slowed down.
- ✓ Have trouble sleeping.
- ✓ Think about death or suicide[7]

The DSM-V criteria for episodes of mania and depression [8]

- An episode of mania must involve a sustained abnormal mood plus three of the following features present (or four features if the patient's mood is irritable rather than elevated) to meet DSM-V* criteria.
- Increased talkativeness.
- Decreased need for sleep, e.g. is rested after three hours sleep.
- Excessive involvement in high-risk activities.
- A major depressive episode is defined by five or more of the following symptoms that are present at the same time, for at least a two-week period.
- Depressed mood is seen almost every day.
- Markedly reduced interest or pleasure in all or almost all of the day's activities.
- Insomnia or hypersomnia nearly every day.
- Feelings of worthlessness or excessive guilt.

MECHANISM OF ACTION OF VARIOUS CLASS OF DRUGS [10]

Phenothiazines

Ex: Chlorpromazine, Fluphenazine, Thioridazine

MEDICATION

Mechanism-Based Classification For Antidepressants [5]

category	mechanism	example	Current classification(if any)
1	Selective blockade of NE reuptake(SNRIs)	DMI, NT amoxapine, moprotiline reboxetine	TCAs
2	Selective blockade of 5-HT reuptake (SSRIs)	Citalopram, fluoxetine, paroxetine, sertraline	SSRIs
3	Nonselective enhancement of NE and 5-HT transmission	IMI, AMI phenelzine, tranylcypromine venlafaxine	TCAs MAOIs

Thioxanthene

Thiothixene

MECHANISM OF ACTION

Blockade of dopaminergic receptors especially D2 receptors more than 5-HT2 receptors

Butyrophenone: Haloperidol

Mechanism of action

Blockade of dopaminergic receptors especially D2 receptors more than 5-HT2 receptors Blockade of dopaminergic receptors especially D2 receptors more than 5-HT2 receptors

Atypicals

Aripiprazole, Clozapine, Olanzapine, Quetiapine, Risperidone, Ziprasidone

Mechanism of action

Blockade of histamine receptor particularly 5-HT2 receptors more commonly than D2 receptors

Lithium

Mechanism of action

Uncertain, suppresses IP3 and DAG signaling

Newer drugs for bipolar affective disorder: Carbamazepine, Lamotrigine, Valproic acid

Mechanism of action

Carbamazepine: Blocks voltage-gated Na+ channels and decreases glutamate release

Lamotrigine: Blocks Na+ and Ca2+ channels, decreases glutamate

Valproic acid: Blocks high-frequency firing.[10]

4	Unknown potent stimulatory effects on NE or 5-HT	mirtazapine trimipramine bupropion nefazodone, trazodone	TCA
5-HT, 5-hydroxytryptamine (serotonin); AMI, amitriptyline; DMI, desipramine; IMI, imipramine; MAOI, Monoamine oxidase inhibitor; NE, norepinephrine; NT, nortriptyline; SNRI, selective norepinephrine		Reuptake inhibitor; SSRI, selective serotonin reuptake inhibitor; antidepressant.[20]	TCA, tricyclic

Marketed Drugs For Bipolar Disorder [9]

Drug name	Generic name	Drug class	Company name	Brand names
Lamictal	Lamotrigine systemic	Triazine anticonvulsants	Glaxosmithk line llc	Lamotrigine
Seroquel	Quetiaine systemic	Atypical antipsychotic	Astrazenica pharms Apotex inc Alkem labs ltd	
Abilify	Aripiprazole systemic	Atypical antipsychotic	Alembic pharms ltd Accord hlthcare	Aripiprazole
Klonopin	Clonazepam systemic	Benzodiazepine, benzodiazepine anticonvulsants	Roche Alembic pharms ltd Apotex inc glaxosmithk line	
Lamotrigine	Lamotrigine systemic	Triazine anticonvulsants	Mylan Aurabindo pharma Cipla Dr reddys	Lamictal, lamictalodt, lamictal cd
Lithium	Lithium systemic	Miscellaneous antipsychotic agents		Lithobid
Latuda	Lurasidone systemic	Atypical antipsychotic	Sunovion pharms	
Depakote	Divalproex sodium systemic	Fatty acid derivative anticonvulsants	Abbvie	
Risperdal	Risperidone systemic	Atypical antipsychotic	Janseen pharms	
Seroquel XR	Quetiapine Systemic	Atypical antipsychotic	Astrazeneca	
Geodon	Ziprasidone systemic	Atypical antipsychotic	Peizer Sandoz inc Mylan pharms	

			Lupin pharm	
Sapharis	Asenapine systemic	Atypical antipsychotic	Forest labs llc	
Zyprexa	Olazapine systemic	Atypical antipsychotic	Lilly	
Clonazepam	Clonazepam systemic	Benzodiazepine ,benzodiazepine anticonvulsants	Roche Teva Watson Sandoz Abbvie	Klonopin
Depakote ER	Divalproex sodium systemic	Fatty acid derivative anticonvulsants		
Tegretol	Carbamazepine systemic	Dibenzazepine anticonvulsants	Novartis Taro pharm inds Wockhards	
Quetiapine	Quetiapine systemic	Atypical antipsychotic	Astrazeneca pharms Aurabindo Alkem labs ltd Alembic pharm ltd	Seroquel, seroquel XR
Divalproex sodium	Divalproex sodium systemic	Fatty acid derivative anticonvulsants	Abbvie Mylan Actavis labs Anchen pharms	Depakote,depakote ER, depakote sprinkles
Gabapentin	Gabapentin systemic	Gama amino butyric analogs	Pfizer pharms Pake davis Alkem labs ltd	
Catapres	Clonidine systemic	Anti adrenergic agents, centrally acting	Mylan Prinston Inc Sun pharm inc unichem	
Bupropion	Buprapoin systemic	Miscelleneous antidepressents,smoking cession agents	Valeantintl Impax labs mylan	
Risperidone	Risperidone systemic	Atypical antipsychotic	Janssen pharms Biopharma inc Apotex inc	Risperdal,risperdal consta, risperdal M-tab
Sertraline	Sertraline systemic	Selective seratonin reuptake inhibitor	Pfizer Apotex inc Aurabindo pharma	

Carbamazepine	Carbamazepine systemic	Dibenzazepine anticonvulsants	Novartis Wockhardt Taro pharms inds	Tegretol, equetro, tegretol XR
Oxcarbazepine	Oxcarbazepine systemic	Dibenzazepine anticonvulsants	Novartis Amneal pharms Sunpharm inds ltd	

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