

*Ministry of Defence*

## **Synopsis of Causation**

# **Bipolar Affective Disorder**

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## **Disclaimer**

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This synopsis has been completed by medical practitioners. It is based on a literature search at the standard of a textbook of medicine and generalist review articles. It is not intended to be a meta-analysis of the literature on the condition specified.

Every effort has been taken to ensure that the information contained in the synopsis is accurate and consistent with current knowledge and practice and to do this the synopsis has been subject to an external validation process by consultants in a relevant specialty nominated by the Royal Society of Medicine.

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# 1. Definition

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- 1.1. Bipolar affective disorder, as defined by the International Classification of Diseases 10<sup>th</sup> edition (ICD 10), is a disorder “characterised by repeated (i.e. at least 2) episodes in which the patient's mood and activity levels are significantly disturbed, this disturbance consisting on some occasions of an elevation of mood and increased energy and activity (mania or hypomania), and on others of a lowering of mood and decreased energy and activity (depression)”.<sup>1</sup>
- 1.2. Manic episodes are characterised by persistently and uncharacteristically elevated or irritable mood associated with increased energy, increased activity, and a decreased need for sleep, racing thoughts and pressured speech (increased in amount and/or speed). Typically, the individual affected will think overly highly of themselves (grandiosity) to the extent of believing that they have especially well developed abilities or a famous identity. There is a loss of normal inhibitions that results in inappropriate social (and sometimes sexual) behaviour, risk taking and a lack of judgement that has adverse consequences either for the individual or others. Perception becomes subjectively increased with colours and sounds, for example, being perceived as more vivid or intense.
- 1.3. For the diagnosis of mania, both the main psychiatric classification systems: International Classification of Diseases 10<sup>th</sup> edition<sup>1</sup> and the American Diagnostic and Statistical Manual (DSM IV)<sup>2</sup> require that the above disturbances should last at least one week (or result in hospitalisation) and cause significant or almost complete disruption of normal work and social activities.
- 1.4. Hypomanic episodes are less severe manifestations of similar behaviours. They may be shorter in duration and are associated with fewer or no adverse consequences and minimal or mild disruption to normal daily function.
- 1.5. ICD 10 requires that disturbances last at least 4 days and cause “some” disturbance of function for the diagnosis of hypomania to be made. DSM IV requires the same duration of symptoms but an “unequivocal change” in function (without stating whether that change should be an increase or decrease).
- 1.6. Depressive episodes are characterised by the core symptoms of persistently low mood, a reduction or loss of interest and motivation, excessive tiredness and lethargy. Associated symptoms are altered appetite and weight, altered sleep pattern (either insomnia or excessive sleepiness), poor concentration and memory, reduced self-esteem and self-confidence, thoughts of life not being worth living, suicidal ideas and/or plans, and various negative, pessimistic or guilty thoughts regarding self and the future. Symptoms persist for at least 2 weeks and usually for much longer.
- 1.7. Mixed episodes are also recognised, whereby symptoms of mania can either alternate with or co-exist with those of depression.
- 1.8. ICD 10 requires two or more episodes of mood disturbance at least one of which was a manic or mixed episode, for the diagnosis of bipolar affective disorder. It does not subdivide bipolar illnesses.

- 1.9. DSM IV makes a distinction between Bipolar I and Bipolar II disorder. Bipolar I requires repeated, significant mood disturbance at least one episode of which has been either manic or mixed. Bipolar II disorder is defined as 2 or more episodes of mood disturbance, at least one of which was a hypomanic episode, without any manic episodes. This use of subtypes of bipolar affective disorder within classificatory systems has developed alongside a notion of bipolar affective disorder representing a spectrum of different illnesses.
- 1.10. There is a need for increased awareness and recognition of Bipolar II disorder. This is particularly important in patients felt to have a recurrent depressive disorder where episodes of hypomania may be viewed by the patient as periods of well-being. This is of concern as the use of antidepressants in patients suffering from Bipolar II disorder may precipitate mania.
- 1.11. Clinical trials of drugs licensed for use in bipolar affective disorder have focused on Bipolar I disorder.

## 2. Clinical Features

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- 2.1. The prevalence of Bipolar I disorder is between 1% and 2%.<sup>3,4</sup> The first episode may occur at any age but typically is most common in teenagers or young adults. There is often a significant delay (mean 8 years) between the first episode and the diagnosis of the disorder.<sup>5</sup>
- 2.2. Half of episodes last between 2 and 7 months (median 3 months).<sup>6</sup>
- 2.3. Bipolar II disorder is a relatively recent concept and less well studied but has a prevalence of between 1.5% and 5%.<sup>7</sup> As with Bipolar I disorder the onset is typically in adolescence or young adulthood (mean age of onset is 18 years) but diagnosis may be delayed for up to 10 years.<sup>5,8</sup>
- 2.4. The sex distribution is roughly equal but men may have an earlier age of onset.<sup>9</sup>
- 2.5. There are high levels of comorbidity with alcohol and drug misuse (up to 50%)<sup>10</sup> and other mental health problems (especially anxiety disorders and eating disorders).<sup>11</sup>
- 2.6. An important complication of the disorder is suicide, with lifetime rates of between 8% and 20%.<sup>12</sup>
- 2.7. There are high rates of family dysfunction, separation and divorce attributable to the effects of the disease.<sup>13</sup>

### 3. Aetiology

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- 3.1. Aetiological factors are best divided into genetic predisposition and various precipitating factors.
- 3.2. **Genetics.** Genetic factors are most important in determining an individual's predisposition to bipolar affective disorder. About 50% of affected individuals have a family history of bipolar affective disorder and the risk that children of affected individuals develop bipolar affective disorder is about 10%.<sup>14</sup> The heritability of bipolar affective disorder is estimated at over 80%.<sup>15</sup> It seems likely that multiple genes each contribute a small amount to this genetic liability.
- 3.3. **Stress.** There is no evidence that traumatic situations or experiences cause bipolar affective disorder, but traumatic and stressful situations can precipitate episodes of illness (both of mania and depression), particularly in the earlier stages of the illness.<sup>16</sup> The day-to-day demands of a pressurised job or interpersonal friction can precipitate episodes of illness and sometimes effective management requires the affected individual to adopt a less stressful lifestyle.<sup>17</sup>
- 3.4. **Sleep.** Disrupted or irregular sleep patterns (or other patterns of social routine such as eating and exercise) can precipitate manic episodes.<sup>16</sup> This may be as a result of a chaotic lifestyle, shift work or travel across time zones. There is some evidence that a disrupted sleep-wake pattern is the final common pathway of other environmental triggers.<sup>20</sup> Maintenance of regular sleep-wake cycles is advocated as a way of reducing the risk of manic relapse.<sup>17</sup>
- 3.5. **Antidepressants.** Use of antidepressants in an individual susceptible to bipolar affective disorder can result in a 'switch' to a manic state, particularly if there is not concurrent use of mood stabilisers. Switch rates vary between about 2% and 5% for SSRIs but are much higher in tricyclic antidepressants.
- 3.6. **Concurrent illness and prescribed drugs.** Episodes of mania can be precipitated by certain illnesses such as multiple sclerosis, brain tumours and hyperthyroidism and also by prescribed medications (such as corticosteroids and L-DOPA). However, these episodes are termed secondary mania and are not necessarily related to bipolar affective disorder. HIV is also a potential cause of mania.
- 3.7. **Childbirth.** The majority of women with bipolar affective disorder are likely to relapse in the postpartum period and even those taking prophylactic treatment remain at significant risk.<sup>18</sup> Abortion can also act as a trigger.<sup>19</sup>

## 4. Prognosis

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- 4.1. The outcome is poor in that repeated episodes are the norm. Patients with bipolar affective disorder have, on average, about 0.4 episodes per year<sup>6</sup> but with a large degree of individual variability. The length of inter-episode euthymia tends to decrease with time.<sup>6</sup> Episodes may occur spontaneously or may be precipitated by the factors described above.
- 4.2. In most individuals, there is good resolution of symptoms between episodes but a significant minority may not attain good functional recovery even after their first diagnosed episode.<sup>21</sup> Patients who have been hospitalised spend about 20% of their life in episodes.<sup>6</sup> Patients with Bipolar II disorder are symptomatic for about 50% of the time.<sup>22</sup>
- 4.3. Traditionally, it has been stated that recovery between episodes is “usually complete,”<sup>1</sup> but more recent evidence indicates that there is persistent cognitive impairment<sup>23</sup> as well as inter-episode morbidity.<sup>22</sup>
- 4.4. Recognition of ‘early warning signs’ (i.e. incipient mania or depression) allows more rapid treatment interventions and better outcome (increased time to relapse).<sup>24</sup>
- 4.5. The goal of treatment for bipolar affective disorder is to use agents which are both efficacious in the acute phases of illness and also serve to prevent relapse into either mania or depression in a “mood maintenance” (also known as “relapse prophylaxis”) phase.
- 4.6. The drugs which are most widely used are:
  - The mood stabilisers (lithium, sodium valproate, lamotrigine, carbamazepine) which are thought to have a role in all phases of the illness
  - The atypical anti-psychotics (which have efficacy in mania and maintenance treatment)
  - Antidepressants (used in depression only, and withdrawn if manic relapse)
  - The benzodiazepines (which have a short-term role to aid sleep).
- 4.7. For refractory depression and mania, ECT remains a treatment option.
- 4.8. Bipolar depression may not necessarily respond to treatment in the same way as unipolar depression and antidepressants should be viewed with caution due to the risks of switch to mania. Studies have shown lamotrigine to be of particular use in this group.
- 4.9. Many individuals may respond well to monotherapy but for some, rational combination therapy (commonly a mood stabiliser and an atypical antipsychotic) is required for an optimal outcome.

- 4.10. Psychoeducation and cognitive therapy are valuable adjunctive treatments during all phases of the illness and can also serve to optimise compliance and facilitate recognition of early relapse.
- 4.11. The prognosis is worse if there is comorbid substance misuse, repeated previous episodes, a history of child abuse or pre-existing poor occupational functioning.<sup>27</sup>
- 4.12. The term “rapid cycling” refers to the course of a bipolar illness rather than a separate diagnostic category. These individuals tend to have 4 or more episodes of illness within a 12 month period and have higher rates of morbidity and treatment resistance. It is associated with treatment with antidepressants as well as comorbid substance abuse, anxiety and the female gender.



## **5. Summary**

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- 5.1. Bipolar affective disorder is a common disorder of mood and behaviour manifested by repeated episodes of mania/hypomania and depression.
- 5.2. Genetic factors are the main causal determinants of bipolar affective disorder but stress and environmental factors (including interpersonal tension, occupational stress and sleep disturbance) are implicated as precipitants of episodes of illness.
- 5.3. The prognosis is poor in that the disease is usually recurrent, although there can be prolonged periods of good health and function between episodes.
- 5.4. There is wide individual variation in the frequency and severity of episodes and their effects on overall function.

## **6. Related Synopses**

Depressive Disorder

## Glossary

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antidepressants	A group of drugs used to treat depression and related disorders.
comorbidity	The occurrence of 2 or more disorders in the same individual. Hence comorbid, of a coexisting disease.
euthymia	A mood state that is neither pathologically elevated nor depressed.
heritability	The proportion of the incidence of a disease that can be attributed to a particular genetic factor.
prophylactic treatment	Treatment used with the aim of preventing illness rather than treating existing illness.
SSRIS	Selective serotonin reuptake inhibitors. A subgroup of antidepressants that are commonly used to treat depression.
tricyclic antidepressants	An older sub-group of antidepressants.

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