

# Biological causes of bipolar disorder psychology essay



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Bipolar disorder is likely one of the most difficult diagnoses to receive in terms of living a normal life. As a psychological disorder, or more specifically, a mood disorder, its typical age of onset is in the early twenties, and its prevalence is between one and two percent worldwide. The disorder is characterized by an alternation between mania and depression, as well as poor impulse control, attention deficits, and impairments of verbal memory. Intensity of the manic state in a bipolar patient determines whether they are diagnosed with bipolar I or bipolar II. Those with classic, full-fledged mania have bipolar I, whereas those with a less extensive version involving anxiety or irritability, sometimes referred to as hypomania, have bipolar II (Kalat, 2013). Causes of the illness are not always clear, but one or a combination of factors such as neurochemical factors, environmental factors, and genetics usually play a part in the development of bipolar disorder (Bressert, 2007).

Genetics are an essential factor, as bipolar disorder is a very biologically based illness. Certain genes have been shown to increase the risk of developing bipolar II disorder, and also some genes associated with a predisposition to major depression predispose to bipolar disorder. However, no definitive relationships exist between these genes and bipolar disorder (Kalat, 2013). Various statistics have been obtained through research as far as chances of developing bipolar disorder based on its prevalence within a family. For example, the risk of the illness is between fifteen and twenty-five percent for those with a parent who has bipolar disorder. Furthermore, the risk for someone whose non-identical twin has the condition is twenty-five percent, which increases eightfold if they are identical twins (Bressert, 2007).

## Biological Causes Overview

Here is an overview of many different factors that are biological in nature and have implications in bipolar disorder, some of which will be explored in further detail later. As a primarily biological illness, the improper functioning of neurotransmitters such as serotonin, norepinephrine, and likely many others has been identified as a cause (Bressert, 2007). Another interesting biological factor includes the brain's increased use of glucose throughout a manic episode and its decreased use of glucose during depressive episodes (Kalat, 2013). Studies analyzing the reelin gene which helps in brain function and development have found that there is a link between the dysfunction of the reelin gene and psychiatric disorders, specifically schizophrenia, and more importantly for this paper, bipolar disorder (Ovadia, 2011).

On a side note, there have also been studies which have found a gene that may provide some sort of protection against bipolar disorder. It is called GRIK4, and as a 'kainate-type ionotropic glutamate receptor' is part of the glutamate neurotransmission process (Pickard, 2006). Another interesting indicator of bipolar disorder was found using sensory gating, and involves the P85 gating ratio (Patterson, 2009).

Relating to the circadian rhythm aspect of the disorder and how disruption of this due to the disorder can be a cause of the manic and depressive states in bipolar patients, there have been some studies. The results of one study found an association between the NR1D1 and GSK3 $\beta$  variants and differences in functioning of the expression of genes related to the 'circadian clock' system (McCarthy, 2011). An association specific to rapid cycling bipolar disorder involves the gene variation of CRY2, a 'clock gene' <https://assignbuster.com/biological-causes-of-bipolar-disorder-psychology-essay/>

(Sjöholm, 2010). A biological marker related to gluten sensitivity has been discovered which showed that those with bipolar disorder have 'increased levels of IgG antibodies to gliadin' (Dickerson, 2011). Finally, a recent study looked into gene expression in lymphoblastoid cells, which could be a possible biological marker of bipolar disorder (Kato, 2011). Overall, it seems that there are still many questions as far as biological causes of the disorder, though progress towards the specifics of those markers is definitely being made.

## **Circadian Rhythm Factors**

The body's natural circadian rhythm is affected in those with bipolar disorder. This has been discovered by McCarthy et al. (2011) through research into the effects of a certain treatment, lithium. It has been shown that lithium affects the function of circadian rhythm with the goal of treating the disorder. Further research conveys issues with functioning of the circadian rhythm that lithium seems to treat. According to one study, positive lithium response is predicted by the combination of variants within  $GSK3\beta$  and NR1D1. This shows that in bipolar patients, lithium affects circadian clock genes, specifically NR1D1 and  $GSK3\beta$ , in an attempt to alter circadian rhythms. Also, a transcription of NR1D1, called Rev-Erb $\alpha$ , functions as a 'clock signaling molecule' which is important as it is degraded by lithium's inhibition of  $GSK3\beta$ . Lithium also can lengthen the natural circadian rhythm and regulate the stability and turnover of proteins within the clock mechanism (McCarthy, 2011). Therefore, it is fairly clear that lithium affects the circadian rhythm of bipolar patients. This is interesting from a biological standpoint so that further research can be done into which

clock genes don't function properly due to the disorder, or if their dysfunction is what causes the disorder.

As Sjöholm et al. (2010) found, rapid cycling in bipolar disorder relates to a specific circadian gene, called Cryptochrome 2 (CRY2), which is a main part of the pathway responsible for the body's roughly twenty-four hour cycle.

Analysis of single nucleotide polymorphisms (SNPs) for associations to bipolar I and II and bipolar with rapid cycling led to analysis of haplotypes only for the rapid cycling cases. Rapid cycling patients were focused on since their circadian rhythms were hypothesized to be more vulnerable.

Haplotypes of CRY2 that indicated risk and protection were discovered in the study of bipolar patients. AAAC and AGGA were haplotypes found frequently in the rapid cycling bipolar patients, and GGAC was a haplotype found much less frequently in rapid cycling patients. This provided evidence for the conclusions that CRY2 is involved in bipolar disorder, and more specifically, which haplotypes lead to protection from or risk of the disorder (Sjöholm, 2010).

Assessment of more clock genes was completed by Yang et al. (2009), in which 'rhythmic expression patterns' were examined and some interesting results were reached. Fibroblasts of bipolar patients and healthy controls were analyzed during the study. The amount of expression for half of the genes being studied, BMAL1, REVERBa and DBP, was less in the bipolar patients than the controls, in addition to the 'mRNA expression levels' in two of the genes, DEC2 and DBP. Next, four kinases were examined for 'mRNA expression levels', and two of the four, GSK3a and GSK3b, were examined for phosphorylation and protein levels. Results were that in GSK3b, the level  
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of phosphorylation was much less in bipolar patients than in the controls. Overall, while nothing is made absolutely clear by this study, there is substantial evidence that circadian genes in bipolar patients are expressed differently than those in mentally healthy individuals. This difference may contribute to dysregulation of other genes down the pathway, which in turn might explain some of the issues that bipolar patients have, relating to their circadian clock (Yang, 2009).

Therefore, circadian rhythms are a main component in bipolar disorder, and the more that becomes understood, the better that aspect of the illness can be treated in the future. For now, it seems to be mainstream knowledge that maintaining a constant sleep schedule can help these symptoms of the disorder, but soon there may be better options for those that suffer with this frustrating disorder (Kalat, 2013).

## **Neurological Factors**

Functional flaws in the neurological systems of bipolar disorder patients are implied in the emotional impairment of those with the illness, according to Phillips et al. (2008). Since regulating emotions is a vital part of being able to function in modern society, bipolar patients are posed with a particularly difficult dysregulation. Neuroscience examining youth development of emotion regulation in their neural systems is key, as advances made in this area could help target predisposed individuals and intervene to possibly prevent the development of bipolar disorder. Structural and functional abnormalities in those with the disorder may be valuable biomarkers with the potential of earlier detection and more successful treatment. This would be a very relevant and applicable result for bipolar disorder specifically, <https://assignbuster.com/biological-causes-of-bipolar-disorder-psychology-essay/>

since it is often discovered once it is too late for a successful treatment plan, or misdiagnosed altogether (Phillips, 2008).

Areas of the prefrontal cortex that are involved in control processes such as regulation of emotions, and decision making are stated by Phillips et al. (2008) and include the “ orbitofrontal cortex (OFC), dorsomedial prefrontal cortex (MdPFC), anterior cingulate gyrus (ACG), dorsolateral prefrontal cortex (DLPFC) and ventrolateral prefrontal cortex (VLPFC)” (Phillips, 2008).

Networks involving the orbitofrontal cortex and the dorsomedial prefrontal cortex allow for coordination of sensory integration and visceral control of prominent emotional information and also assist emotional behavior regulation. The amygdala is also connected to the orbitofrontal cortex and anterior cingulate gyrus according to a study by Ghashghaei et al. (2007), with implications involving focus on ‘ motivationally relevant stimuli’. Studies have also shown less activity in the left side of the ventrolateral prefrontal cortex, specifically in ‘ automatic emotion regulation’ involved regions, throughout mania and remission in bipolar adults. Also, significantly reduced activity within the left sides of the dorsomedial prefrontal cortex and the orbitofrontal cortex throughout automatic attention and emotion regulation in bipolar adults. Overall, the neurodevelopment of bipolar disorder is quite obviously complex, but it is evident that abnormalities in regions of the left side prefrontal cortex as well as the left side hippocampus and parahippocampus, at least in childhood bipolar disorder, are present and should be further examined. (Phillips, 2008).

According to Craddock et al. (2010) after analysis of a ‘ Wellcome Trust Case Control Consortium’ study, a gene that encodes the ‘ GABA receptor  $\gamma 1$ ’  
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subunit, GABRB1' contained a significantly associated polymorphism, based on an analysis of bipolar patients and controls. After further studies they determined that variation within the GABA receptor genes can contribute towards risk of bipolar disorder. Therefore, this is yet another implication of a neurologically related issue in bipolar disorder patients, this time concerning a factor that could be related to alcohol issues and things of that nature in those with bipolar disorder (Craddock, 2010).

According to Yuan-Hwa et al. (2010), midbrain binding of serotonin transporter (SERT) has been shown to be decreased in those in the depressive state of bipolar disorder in previous ' positron emission tomography studies'. In the study completed by Yuan-Hwa et al., the goal was to analyze if the same dysfunction would apply to those in the euthymic state of the disorder. The study was conducted by using two rating systems, the ' Montgomery-Asberg Depression Rating Scale' and ' Young Mania Rating Scale', with a less than ten score or less than seven score, respectively, over an eight week period classifying a euthymic state. To measure the midbrain binding of serotonin transporter, Yuan-Hwa et al. used ' single photon emission computed tomography' and the ' radiotracer 123I-ADAM'. Representing the availability serotonin transporter binding within the midbrain, the main outcome measured was ' specific uptake ratio (SUR)' (Yuan-Hwa, 2010).

Results included dramatically lower averaged specific uptake ratios for bipolar I patients than for bipolar II patients or healthy individuals according to Yuan-Hwa et al. (2010). There was also a strong correlation of decreased specific uptake ratios in bipolar I patients with illness duration. This means

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that there is a different biological regulation mechanism in bipolar I patients than in bipolar II patients following stable treatment, which could make a case for dichotomy in bipolar disorder (Yuan-Hwa, 2010).

Overall, neurotransmitters and other neurological system factors play a large role in understanding bipolar disorder of various types and could potentially lead to diagnosis and treatment of the illness earlier rather than later, when it has the best chance at being successful. If one thing is clear related to the neurological piece of this bipolar puzzle, it is that abnormalities and decreased levels of functioning are present, and need to be further understood if progress toward better management of this disorder is going to take place.

## **Miscellaneous Factors**

There are many other various factors that have biological implications in bipolar disorder. In this section, they will be discussed one by one. From protective factors to biomarkers that may increase risk, they will be explored in detail.

The first factor concerns a certain ' kainate-type ionotropic glutamate receptor' that is part of the glutamate neurotransmission process, called GRIK4, according to Pickard et al. (2006). Regarding bipolar disorder, a two single nucleotide polymorphism haplotype of the gene proved to be the most significant. Results regarding the haplotype inferred a protective quality towards bipolar disorder. Also, Pickard et al. identified multiple individual haplotypes from markers four to eight, which subsequently associated with a protective quality regarding bipolar disorder, even though that region did not

appear within the ' global analysis' (Pickard, 2006). Therefore, it is clear that this gene has properties which protect the individual from developing bipolar disorder.

Regarding the reelin gene (RELN), which helps in brain function and development, Ovadia and Shifman (2011) have found that there is a link between the dysfunction of the gene and psychiatric disorders like bipolar disorder. The expression of the reelin gene and its various isoforms was studied using brain samples from postmortem patients of bipolar disorder and schizophrenia. Results indicated that there was a discernible reduction in the short reelin gene isoform proportion, which was lacking the ' C-terminal region', in bipolar disorder. Hence, the RELN, or more specifically its short isoform, is dysfunctional and that dysfunction can be associated with bipolar disorder (Ovadia and Shifman, 2011).

Patterson et al. (2009) found a biological marker of bipolar disorder using sensory gating, and specifically the P85 gating ratio. Their goal was to discover if and how gating of an ' auditory brain potential at 85 ms' (P85), which hadn't been previously tested, differentiated patient groups and control groups. Patterson et al. collected ' P85 and P50 auditory evoked potentials' from schizoaffective disorder patients, paranoid schizophrenia patients, and bipolar I disorder patients, and also from healthy control individuals. The results showed that the P85 gating ratio was dramatically greater in the bipolar group compared to any of the other groups; and the P50 gating ratio was dramatically greater in the schizoaffective group than it was in the control group, however it didn't differ from the ratio for the paranoid schizophrenia group or the bipolar group. Therefore, given the <https://assignbuster.com/biological-causes-of-bipolar-disorder-psychology-essay/>

results, the P85 gating ratio might be a unique new biomarker for bipolar disorder (Patterson, 2009).

“ BD is associated with a number of genetic and possibly epigenetic abnormalities associated with neurotransmitter, hormonal and immunologically mediated neurobiological pathways...HPA axis and immune system abnormalities...” (Duffy, 2012). This study completed by Duffy et al. basically reviews various biological indicators pertaining to susceptibility to bipolar disorder. Certain studies examined differences in the ‘ hypothalamic-pituitary-adrenal (HPA) axis’ and also the immune systems of bipolar patients. In addition, there were implications to bipolar disorder found involving ‘ signal transduction processes’ within cells and also disruption within ‘ energy metabolism’. Individuals at genetic risk provide a context for neurobiological findings and models concerning the onset and the progression of the illness are discussed. Overall, neuronal systems are dysfunctional in some ways in those with bipolar disorder, and because of this, things such as apoptosis concerning the strain of the disorder and oxidative stress can occur, which obviously are not normal or healthy in any way (Duffy, 2012).

Going in a little different direction, Kapczinski et al. (2009) studied recurrence of manic and depressive episodes and how it can contribute to the progression of the disorder. Neurobiological abnormalities may increase as episodes happen over and over, and as the number of episodes an individual has had increases, both treatment by medicine and by psychotherapy become less and less successful. This may be due to worsening dysfunction regarding insight, cognition, and relationships, and <https://assignbuster.com/biological-causes-of-bipolar-disorder-psychology-essay/>

various other types of functioning. Also, the degree to which the illness has progressed can be assessed by the continuation of dysfunctioning throughout the fairly normal mood phases that bipolar patients experience (Kapczinski, 2009).

Various indicators for bipolar disorder include, "...abnormalities in some biomarkers, such as brain derived neurotrophic factor (BDNF) and cytokines such as tumour necrosis factor alpha (TNF-alpha), which may be related to neuronal and glial dysfunction" (Kapczinski, 2009). These specifically are relevant to the possible staging of the disorder as increased levels of ' TNF-alpha' and decreased serum levels of ' BDNF' characterize patients in the later stages of the illness when examined in relation to those in the earlier stages. Therefore, if studies are replicated and more evidence supports differences significant enough to classify stages of bipolar disorder with unique treatment options and things of that nature, patients may not need to suffer unnecessarily and more success can be achieved towards the goal of relatively normal lives for these individuals (Kapczinski, 2009).

## **Conclusion**

To conclude, there is much that has yet to be discovered regarding the causes and various indicators, biological and otherwise, of bipolar disorder. However, progress is most definitely being made, and there are many promising avenues to pursue in terms of achieving a greater understanding of this illness and how it is developed. From genetics and neurotransmitters which clearly play a significant role, to circadian rhythm factors which seem to be quite valid, this disorder has many influences.

While it may seem at first to be a disorder triggered by environmental factors and various life events, it really is heavily biologically incorporated into those who suffer from this life altering and sometimes uncontrollable illness. As more studies are completed that test for various abnormalities, dysfunctions, and possibly even new types of differences within individuals who have bipolar disorder and those likely prone to developing it, more factors will be discovered and it is more than likely that a better grasp on the complexities of the illness are not too far away. To put it simply, though patients of this disorder may feel hopeless and beyond frustrated at times, researchers do not, and the day when the illness is entirely understood and treatment options are consistently effective will come sooner than some people might think.