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The Role of Dopamine in Mania in Bipolar Disorder

ABSTRACT

Background

Mania is a temporary period of abnormally elevated or irritable mood in individuals with bipolar disorder. During this time, an individual experiences a significant difference in their thoughts, feelings, and actions from their typical disposition during euthymia.

Objective

This review investigates the role of dopamine in mania in order to better understand how manic episodes are expressed in individuals with bipolar disorder.

Methods

A PubMed search was conducted using the keywords “dopamine”, “mania” and “bipolar disorder,” and a total of 5 studies done on dopamine in mania were included for this review article.

Results

The studies included in this review found that during mania, dopamine levels were elevated in the brain and when dopamine levels increased in participants not experiencing mania, it led to manic-like symptoms and behaviors. Manic behavior was observed in both mice models and human participants. These increased levels were caused by a shortage in dopamine transporters.

Conclusion

This review emphasizes the significant role that dopamine plays in mania in bipolar patients. Specifically, increased amounts of dopamine or a lack of DAT in the striatum causes mania and heightens its severity with increasing amounts of dopamine.

INTRODUCTION

Bipolar Disorder is a diagnosed psychiatric disorder in which an individual experiences prolonged periods of depression and mania when not in a euthymic (stable) state [1]. This paper focuses on mania, which is commonly known as an intense elevation of mood and energy for a temporary period in which the person is abnormally irritable, ecstatic, or easily aggravated [1]. Mania is differentiated from a normal hormonal mood swing because of its extreme nature and prolonged period of expression.

In the last three decades, bipolar disorder diagnoses have been rising [1]. With increased incidence, a significant amount of research has been pursued to understand the chemical and structural changes underlying the disease, including the role of dopamine. Mania, in part, is driven by changes in dopamine levels. Research has shown that manic episodes can be triggered by medications or drugs that increase dopamine activity while blocking dopamine receptors and reducing activity can help stabilize mood and control mania [2]. By the general public, bipolar disorder has been confused in the past with dissociative identity disorder, which is characterized as a mental health condition that causes a person to believe they have multiple personalities or identities [3]. Bipolar disorder is not a switch in identity but rather a drastic change in mood, likely influenced by dopamine as one of the neurotransmitter's main functions is to act as a mood regulator. Recently, as the medical industry gains more means to track dopamine levels in the striatum via scans such as PETs and MRIs, the correlation between dopamine and manic behavior has become more evident [4-6].

The focus of this paper is to observe the role of dopamine in individuals with bipolar disorder when they express signs of mania. Through understanding dopamine's function and its activity in the brains of individuals undergoing a manic episode, this review prompts the recognition of how important dopamine is to treat and manage manic episodes in individuals with bipolar disorder. The research synthesized in this article provides possibilities for future treatment, including insight into how modulating dopamine function in bipolar disorder may address manic episodes.

METHODS

This review was conducted by searching Pubmed to identify articles exploring the association between dopamine and bipolar disorder. Keywords included "dopamine," "mania," and "bipolar disorder." Reviews and case studies were excluded.

RESULTS

A total of five studies were included in this review, including two studies using mice models and three studies with human participants. Across the studies included in the review, PET scans were a popular method of detecting dopamine levels in the brain in humans, tying high levels of dopamine to the expression of mania or symptoms of mania in bipolar disorder [4-6]. In many of these studies, dopamine transporters (DAT) were decreased in patients with bipolar disorder compared to healthy participants [4, 7, 8].

Dopamine's impact on mania was significant when dopamine levels themselves were higher in the brain or when DAT were lower. All the studies agreed that with raising dopamine levels in the brain, specifically in the striatum, signs and behaviors that accompany mania were often observed. These behaviors included, but were not limited to, increased numbers of premature or impulsive decisions, increased motivation, and excessive switching in choices during reward processing, hyperactivity, and repetitive movement patterns [7, 8].

Table 1 is a summary of the objectives, participants involved, conclusions, and relevance of each study on the role of dopamine in mania. The review includes studies done on mice as well as studies done on humans to see how changes in dopamine levels influence individuals with bipolar disorder.

Table 1. Summary of studies on the significance of dopamine in manic episodes in bipolar disorder

Study	**Objective**	**Participants**	**Main Conclusions**	**Relevance to Question**
Young et al., (2016) [7]	This study was done to link DAT reduction to manic episodes in patients with diagnosed bipolar disorder.	45 regular mice and 55 13 month old Dopamine Transporter Knockdown (DAT KD) male mice with their wildtype (WT) littermates.	Administering GBR 12909 (an inhibitor of dopamine intake) to normal mice and using DAT KD mice produced behavior similar to patients with mania. While lithium reduced these effects, it didn't reduce dopamine levels, rather regulating the way the brain processes	This article indicates that increased dopamine levels in the brain cause mania-like behavior. When giving mice more dopamine, mania-like behavior was induced, suggesting that an excess of dopamine in the brain is a main cause for occurrences of mania.

			hyperactive dopamine signals.	
Yatham et al., (2022) [4]	The purpose of this study was to assess DAT density in the striatum and its connection to mania frequency and severity.	9 patients diagnosed with Bipolar Disorder in a current manic episode, 17 that were treated for one recently, and a control group of 21 healthy people with no history of psychiatric disorders or family history of mood disorders.	People with current mania or recent manic episodes showed significantly lower dopamine transporter binding potential in the striatum compared to healthy control individuals. Within bipolar patients, those with current mania had even lower levels of DAT BPND than those that had recent episodes but are stable currently. The correlation shown between mania and dopamine was that lower DAT created higher symptoms of mania.	This study emphasizes that lower DAT levels in the striatum, which causes an excess of dopamine, increases symptoms and behavior associated with mania. This supports the theory that dysregulation of dopamine is an underlying cause for manic episodes and often prompts the occurrence of mania.
Jauhar et al., (2025) [5]	This study was performed to test for dopamine synthesis capacity variety between affective syndromes across psychotic disorders and its correlation with psychotic	Patients with first-episode psychosis and mood disorders: 76 participants were studied, 25 with major depressive episodes [MDE], 13 with mixed/mania, and 38 controls.	MDE patients had lower striatal dopamine synthesis than mixed/mania patients, particularly in the limbic striatum. MDE differed from the controls, but mixed/mania did not. A higher Kicer, striatal	This relates directly to my paper because this study deals with neuroimaging evidence in humans that overactivity of dopamine or dopamine dysregulation has a major influence in mania and the

	symptom severity.		dopamine synthesis, was associated with more severe positive psychotic symptoms, strongest in the associative or sensorimotor striatum, but not in the limbic striatum.	severity of its symptoms. Essentially, dopamine overactivity or dysregulation in the striatum is one of the reasons for behavioral and cognitive symptoms or features of bipolar mania.
McCutcheon et al. (2021) [6]	This study's aim was to find out how dopamine receptors found in the striatum are linked to other parts of the brain and how that link is influenced by genes.	All participants were over 18 and had no past or current major medical conditions, a history of neurological or psychiatric disorders, history of a head injury with unconsciousness, family history of psychiatry in first-degree relatives, or difficulties with PETs, MRIs, or amphetamine.	When the patients were administered amphetamine, changes in the striatal dopamine were linked to changes in cortical blood flow, and the pattern of this link could be predicted by certain genes. The genes they found that could predict these patterns of correlation were involved in brain signaling as well as cognition, of which some are heavily involved in bipolar disorder, schizophrenia, and autism.	This relates to my research question by providing evidence that if the relationship between dopamine patterns in the striatum and blood flow patterns in the cortex is warped or upset, it often leads to the development of psychiatric disorders.
Young et al., (2009) [8]	The point of this study was to create a model of bipolar disorder mania in mice and	Four month old male 29/SvJ mice and C57BL/6J mice	Amphetamine and GBR 12909 both caused increases in activity and changes in behavior that	This suggests that when dopamine is increased, mania-like behavior is induced,

	disrupt dopamine activity through the restriction of DAT function to see if that produces a mania-like episode	that were group-housed.	induced mania-like symptoms such as hyperactivity and repetitive movement patterns.	highlighting the role dopamine plays in mania in bipolar disorder. Higher levels of dopamine activity increase manic episodes and their severity, while lower levels of dopamine activity create a more stable mood and decrease symptoms of mania.

DISCUSSION

This review addressed the role of dopamine in manic episodes in patients with bipolar disorder, specifically looking at how a surplus of dopamine or a shortage of dopamine transporters (DAT) induces mania or manic behavior. This was done through combining the results of multiple studies involving dopamine levels in the brain. The studies included in this review reveal a correlation indicating that when dopamine levels in the brain are increased, manic-like behavior is displayed. In certain studies, participants were observed during manic episodes to measure dopamine frequency in the brain while mania was occurring [4], while in others, manic behavior was observed as a result of increased dopamine [7, 8].

Though many of these studies were not performed only or specifically on participants diagnosed with bipolar disorder, all were related to the condition in some way. In one study using mice models, Jared W. Young found that when administering GBR12909, a highly selective inhibitor of dopamine uptake and a blocker of DAT, it led to increased motivation, hyperactivity, and the tendency to make more impulsive choices, similar to symptoms common in bipolar mania [7]. The exhibition of these behaviors when given GBR12909 supports that increased dopamine levels in the brain cause mania [7].

In another mice model study done by Young, the same GBR was administered to the mice, and they were observed to have higher activity and predictable movement patterns [8]. Patients with bipolar disorder express these symptoms as well, and Young was able to relate the symptoms shown in these mice with psychiatric disorders such as schizophrenia and bipolar disorder [8].

In other studies, experiments were done with PET imaging or MRI scans to measure dopamine in the brain during mania [4, 5, 6]. Sameer Jauhar used 18F-DOPA PET imaging to detect dopamine activity in patients with Major Depressive Disorder (MDE), mixed/mania, and a

healthy control group [5].A lower Kicer, which is a measure of striatal dopamine synthesis capacity, was found in patients with MDE while in the mixed/mania group, a higher Kicer was observed than in the control and MDE participants [5]. A higher Kicer was associated with more severe psychotic symptoms, reflecting how producing more dopamine in the striatum leads to behaviors associated with bipolar mania [5].

Another study using PET scans was performed by Lakshmi N Yatham, who used the PET to document DAT density in patients with current mania, recent mania, and healthy patients with no history of manic behavior.[4]. Within the bipolar diagnosed participants, current manic individuals' DAT BPND was even lower than those who had experienced mania recently but were stable currently [4]. The participants who had recent mania experienced smaller reductions primarily in the left striatum [4]. The correlation observed was that lower DAT created more severe symptoms of mania [4].

A study by Robert A McCutcheon, also using PET scans, attempted to find how dopamine receptors in the striatum are linked to other parts of the brain [6]. The study revealed a clear connection between the location of dopamine receptors in the striatum and cortical blood flow [6]. The patients were administered amphetamine and changes in striatal dopamine were linked to changes in blood flow in the cortex [6]. They found that genes involved in brain signaling and cognition could predict the patterns of dopamine and cortical blood flow relations [6]. These genes are also significantly involved in bipolar disorder, schizophrenia, and autism [6]. The study revealed that dopamine affects brain activity in the cortex, prompting the idea that if this system is disrupted, it is linked to the development of psychiatric disorders [6].

A recurring theme throughout all studies was that increased dopamine induces mania, whether looking at human or mice models [2, 4-8]. There were no disagreements throughout all sources when it came to their central results, with all concluding that higher levels of dopamine in the striatum is associated with mania [2, 4-8].

Dopamine levels rising in manic patients or inducing manic behavior is likely due to the neurotransmitter's role in reward processing and pleasure systems. Dopamine is known to be the happy hormone, reflecting its function as a mood regulator, but in mood disorders like bipolar disorder, dopamine is not at its regular levels [2, 4-8]. When dopamine increases, it causes mania/manic symptoms because it leads to euphoria or feelings of ecstasy, giving the brain a false illusion of being able to accomplish unrealistic goals. As a result, in mania, patients have an increased tendency to take risks and make impulsive decisions. The symptoms seen during mania can vary, from elevated mood, distorted sense of self confidence, hyperactivity, and reduced sleep to low attention span and poor decision making [7, 8]. Most of these symptoms were observed as a result of an overabundance of dopamine in the striatum because dopamine's main functions are regulating mood, motor control, and the support of cognitive processes such as memory and decision making skills. With an excess of dopamine comes the dysregulation of these functions, inducing mania because these processes are not controlled to the appropriate

extent. As dopamine increases or DAT decreases in the brain, all its functions are overperformed, so the patient's mood becomes unnaturally high and they display aggression and impulsivity.

As bipolar disorder diagnoses have increased globally since 1990, especially among adolescents and young adults, it is important to understand what causes its symptoms and what systems in the brain contribute to it [1]. Dopamine's role in mania is highly significant, as it can also provide options for future treatments. Furthermore, by seeing how dopamine transmission varies in mania, regular mood swings exhibited by adolescents can be distinguished from manic episodes in bipolar disorder. The inability to recognize manic episodes often leads to the dismissal of bipolar patients, especially within families. Understanding dopamine's role in the disorder can help patients get the treatment and help they deserve.

One explored treatment option in a study was lithium treatment, which regulated the brain's ability to process hyperactive dopamine signals [7]. While lithium was able to effectively regulate processing dopamine signals, it wasn't able to reduce impulsive decision making [7]. In the future, these limitations should be studied so lithium treatment and medication is more impactful and helpful to patients. In another study, the idea of using genes that predict the relationship between dopamine signaling and cortical blood flow to treat psychiatric disorders was proposed [6]. This specific study didn't elaborate on how exactly this could be used, but it appears to be a promising new way to treat mania or predict the way the brain will respond to treatment [6]. Ultimately, all studies used in this review agreed that increased dopamine causes mania. More research on how this increase in dopamine is created should be pursued to figure out how to regulate dopamine levels so patients diagnosed with bipolar disorder may be treated earlier and more efficiently.

Overall, while the role of dopamine in mania is that increased levels of dopamine in the striatum contribute to the symptoms and severity of mania, more research should be conducted on why this relationship occurs and how to treat it more efficiently.

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