The International Conference on Interdisciplinary Humanities and Communication Studies
DOI: 10.54254/2753-7048/6/20220232

Abnormality of Reward Sensitivity in Major Depressive Disorder and Bipolar Disorder

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Abstract: Bipolar disorder (BD) and major depressive disorder (MDD) are two major psychiatric disorders that both involve a reward system abnormality. This paper reviews studies on the hyper/hyposensitivity model, also known as the Behavior Approach System (BAS), that emphasize the role of abnormal reward processing in patients with BD and MDD. The paper concludes that BD patients' extremely high reward sensitivity causes manic-related symptoms as well as bipolar depressive symptoms. On the contrary, MDD patients' extremely low reward sensitivity leads to unipolar depressive symptoms such as anhedonia and loss of motivation. Furthermore, this paper discusses the hyper/hyposensitivity model's utility in three areas: how it can aid in disease differentiation and prediction, and how it can be used to develop potential treatments. Because reward sensitivity can be measured using reward tasks, predicting the onset of BD and MDD, making the correct diagnosis, and developing treatments will be easier if the relationship between sensitivity and diseases is clear.

Keywords: reward, major depressive disorder, bipolar disorder

1. Introduction

Recently, an increase in the number of studies on reward-related dysfunction indicates a growing interest in the role of reward sensitivity in the development of psychiatric disorders [1]. People are beginning to realize the possibility of a relationship between abnormal reward systems and the onset of mental diseases such as bipolar disorder (BD) and major depressive disorder (MDD) [2]. Though many studies are exploring this area on the frontline, there are limited papers reviewing important findings and systematically backing the model. This paper, through a method of literature review, concludes and discusses the hyper-hyposensitivity model in four parts. Firstly, the paper explains the reward sensitivity model, also known as the Behavior Approach System (BAS). Then, the paper reviews articles about the reward hypersensitivity model in BD and its research evidence. Third, articles and evidence about the hyposensitivity model in MDD are reviewed. Fourth, it discusses the usefulness of the hyper/hyposensitivity model in three aspects: how it can help in distinguishing and predicting diseases; how it can be used to develop possible treatments; and This review will go over the basic findings of previous studies on the reward hyper-or hyposensitivity model, as well as potential future research directions.

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2. Reward System/Behavioral Approach System (BAS)

According to the Behavioral Approach System (BAS), the reward system is responsible for regulating motivational approaches and behaviors to achieve the goals, and both internal (e.g., reputation) and external (e.g., money) reward cues can activate this system [3]. BAS activation induces striving motivation toward the goal and produces positive feelings when we successfully win the reward. Also, when we fail to get the prize, BAS makes us feel upset and even arouses angry emotions [3]. When looking into the BAS model, the fronto-striatal neural circuit is the most important neuronal structure[4]. This circuit contains dopaminergic projections from midbrain nuclei to cortical target regions, such as the orbitofrontal cortex (OFC), which lead to a series of sensations and behaviors related to reward [4-5]. The central part of the fronto-striatal neural circuit is the ventral striatum (VS). Exposure to reward stimuli increases striatal activity, and many factors, such as reward magnitude, effort amount, and interval time, modulate this activation [4]. The concept of reward sensitivity is closely related to VS activation. When facing reward-related conditions, people who have elevated VS activity are marked as having higher reward sensitivity [4]. Different reward sensitivity levels vary across people, and different reward sensitivities lead to different reward-related behaviors and sensations. For example, research shows that adolescents tend to have higher reward sensitivity compared with children and adults. The high reward sensitivity makes adolescents think the rewards are more attractive and causes them to engage in more risky behaviors to approach the rewards [6].

Along with the normal variance in reward sensitivity, there are also people with abnormal reward sensitivities. Their reward systems either abnormally activate or deactivate when facing reward-related cues. People with excessive reward sensitivity have their reward system overactivated, resulting in hypomania or mania symptoms; people with excessively blunted reward sensitivity have their reward system deactivated, resulting in depression symptoms such as anhedonia [6]. In the next two parts, the author will specifically review and present articles about these two opposite endpoints of reward sensitivity.

3. Reward Hypersensitivity Model in Bipolar Disorder (BD)

Bipolar disorder (BD) is a common psychiatric disease with a 4.4% prevalence rate among the US population [3]. It is characterized by repeated extreme mood swings between mania (or hypomania) and depression. Because of the influence of the disease, BD patients face significant impairment in work, family, and emotions, which leads to an extremely high unemployment rate, divorce rate, and suicide rate (nearly one out of every five BP patients) [5]. Therefore, researchers work to understand the latent mechanism of BD, which can help to develop effective treatments for BD.

The reward hypersensitivity model posits that the reward hypersensitivity of BD patients is the reason for both manic (or hypomanic) symptoms and bipolar depression symptoms [4]. It is not a bad thing to have high reward sensitivity. People with high reward sensitivity tend to feel that reward is more appealing, and they strive to achieve their goals. However, if their reward sensitivity is extremely high, according to the reward hypersensitivity model, they tend to have excessive approach motivations [4]. This tendency leads to manic (or hypomanic) symptoms such as less need for sleep, irritable mood, overconfidence, and elevated psychomotor activation (see the red pathway in Figure 1) [5]. At the same time, since their excessive want to get the rewards, when they have trouble getting the reward or when the reward is deprived, they will develop depressive symptoms due to the excessive deactivation of reward system activation (see the light blue pathway in Figure 1) [4, 6]. In other words, reward hypersensitivity creates lability. When this liability meets the reward attainment conditions, BD patients become overactive and have manic (or hypomanic) symptoms;

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when this liability meets the reward nonattainment conditions, their reward system becomes extremely deactivated, which leads to depressive symptoms [6].

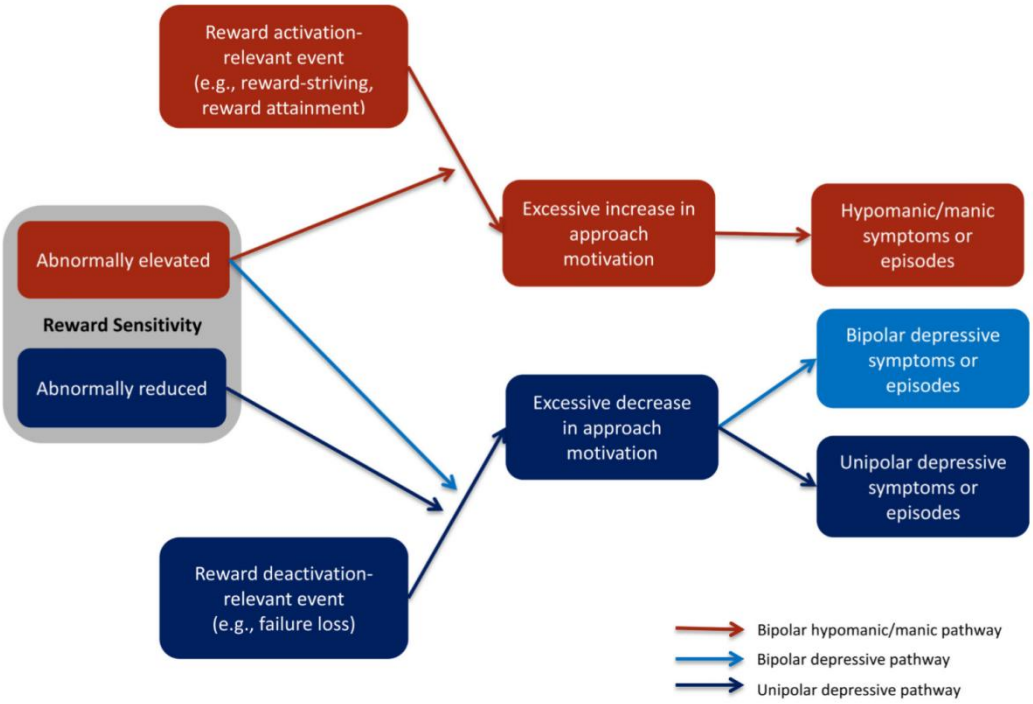

Figure 1: Reward sensitivity model [5].

There is quite some research evidence to support the reward hypersensitivity model in BD. Functional MRI (fMRI) research shows that BD groups have more intense neural activation in the fronto-striatal circuit when approaching reward stimuli compared with healthy participants [3, 7]. When BD patients do a reward anticipation task under fMRI, they show a different neural activation pattern from the healthy control group [8]. During the period of manic and hypomanic symptoms, the brain region with high dopamine receptor density is detected to have heightened activation under reward stimuli. When BD patients anticipate the reward, they show higher activation in the amygdala under no-stress conditions and a lower activation under stress conditions [9]. This finding supports the two opposite possible outcomes (hypo/manic and bipolar depression) in the reward hypersensitivity model. Additionally, Ibanez et al. found that the BD group responded more to reward magnitude but ignored reward valance compared with healthy control in the lowa gambling task [10]. In emotional, behavioral, and cognitive perspectives, BD patients have shown increased reward responsibility [3]. Researchers find that in reward settings, the BD group has increased left-frontal EEG activity, which indicates higher approach motivation toward rewards. Although the amount of elevated activity depends on their status (e.g., manic, hypomania, depression), when BD people are in their euthymic state, they still report relatively high reward sensitivity [3]. Besides EEG evidence, the feedback negativity (FN) component of event-related brain potential (ERP) also shows that BD is related to a neurohypersensitivity toward rewards [5].

4. Reward Hyposensitivity Model in Major Depressive Disorder (MDD)

Different from the two extreme endpoints (hypo/manic and depression) of BD, MDD is a unipolar depression which only contains negative symptoms. A person with MDD is characterized by a continuous depressive mood, decreased emotional arousal, and a loss of interest in activities.

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Among different aspects of MDD, reward-related symptoms, such as anhedonia and lack of motivation, are important in both diagnosis and treatment [11].

According to the reward hyposensitivity model, MDD is the result of abnormal reward hyposensitivity due to the dysfunction of the fronto-striatal neural circuit [11]. When people with low reward sensitivity endure reward deactivated reward events, they tend to have less approach motivation (see the dark blue pathway in figure 1) [4]. As a result of reward hyposensitivity, MDD patients show blunted responses to both reward and punishment [14]. In their behavior pattern, they are less willing to make an effort to obtain the potential reward and less pleasurable when obtaining rewards, which leads to depressive symptoms such as loss of motivation and anhedonia1.

Research provides evidence for the reward hyposensitivity model. In behavior tests, MDD people make fewer risky decisions at a slower speed and are less willing to put effort into rewards compared with healthy controls [4]. In terms of neurology, MDD patients have a blunted striatal response to reward stimuli [12-13]. Using fMRI, negative reward processing is found in the hippocampus and rostral ACC in the MDD group, while the control group shows positive activation in these brain regions [13]. A study of EGG activity also shows that MDD patients have decreased left frontal EEG activity when facing reward stimuli [3]. Moreover, even in fully remitted people with a history of MDD, this reduced EEG activity still exists [4, 11].

5. Discussion

The reward hyper-or hyposensitivity model is useful in several ways. First, it can help to distinguish BD from MDD. Since BD has both hypo/manic and depressive episodes, it is always misdiagnosed as MDD in the first place, which causes incorrect treatment and poor outcomes [14]. However, since BD patients tend to have overly high reward sensitivity and MDD patients have low reward sensitivity, measuring patients' reward sensitivity levels can be a promising method to distinguish BD from MDD [3]. For example, when doing reward tasks under fMRI scanning, BD patients show reduced activation of brain regions, such as NAcc, caudate nucleus, and thalamus, compared with MDD patients [14]. One fMRI study indicates resting-state connectivity strength at multiple reward network nodes has a different pattern between the BD group and MDD group [15]. Another study shows that reduced left frontal EEG activity may be a marker of unipolar depression but not bipolar disorder [5]. However, which neuromarkers are effective to distinguish BD from MDD is still uncertain and needs more research evidence.

Second, we can use the reward sensitivity level to predict BD and MDD. Since sensitivity levels are trait-like profiles that do not vary due to different mental states, abnormal reward sensitivity is likely to be a vulnerability to these mental diseases [3, 8]. Specifically, research shows that reduced reward-approaching motivation and blunted response are linked to the onset of MDD. This finding suggests that we can use reduced left frontal EEG activity as a neuro marker that predicts MDD [6]. Lucking also suggests that blunted striatal response might be a possible predictor of unipolar disorder [16]. For BD, many studies show that the risk can be predicted by investigating the elevated activation in the fronto-stratal reward circuit in reward settings [5, 6, 17]. Additionally, the magnitude of hypersensitivity was correlated to the severity of the BD course [5]. Thus, the vulnerability of developing BD and MDD can be predicted through reward sensitivity markers.

Third, the reward hyper/hyposensitivity model might be useful in developing treatment methods. According to the model, since the cause of BD is the abnormal hypersensitivity of the reward system, treatments focusing on decreasing reward sensitivity might be an effective treatment. Bertocci et al. suggest that the Transcranial Direct Current Stimulation (tDCS) technique can work to decrease reward hyperactivity and negative affect, which might help to treat BD [7]. However, there is limited evidence about the treatment in the reward sensitivity area. Whether it can be an effective treatment for MDD and BD still needs to be figured out.

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6. Conclusion

The reward hyper-or hyposensitivity model describes patients with BD and MDD who have abnormal reward sensitivity. This review aims to explain the model in detail and conclude with supporting evidence found in studies. The extremely high reward sensitivity in BD patients leads to manic-related symptoms and bipolar depressive symptoms. On the contrary, the extremely low reward sensitivity in MDD patients causes unipolar depressive symptoms such as anhedonia and loss of motivation. Since reward sensitivity can be measured through reward tasks, if the relationship between sensitivity and diseases is clear, predicting the onset of BD and MDD, making the correct diagnosis, and developing treatments will become easier. However, this review still has some limitations. Since there are a limited number of papers reviewed here and some of the results of the reviewed studies are inconsistent, it is still hard to conclude that the role of reward sensitivity is clear enough. Future studies can focus on the mechanism of abnormal reward sensitivity, especially in BD, since there are debates about how reward hypersensitivity can lead to two extreme endpoints. Furthermore, testing the relationship from a neurological standpoint and further developing the reward hyper-or hyposensitivity model could be a promising future for research.

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