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The Influence of stress factors on anxiety and depression: The mediating role of neural responses to errors and rewards

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Abstract. This paper examines how stress impacts depression and anxiety through neural responses to mistakes and rewards. Currently, mental health problems, specifically anxiety and depression, are on the rise. This paper presents a study on how stress affects depression and anxiety. To begin with, this paper describes two neural responses: Error-Related Negative Wave (ERN) and Reward Positive (RewP). ERN could be a significant biomarker of anxiety symptoms. RewP, however, is linked to depression. Based on previous studies, this paper posits that depressed patients exhibit lower RewP amplitude indicative of reduced sensitivity to rewards. Moreover, this paper combines previous studies to demonstrate that stress could impact the amplitude of ERN and RewP. To be more precise, stress could amplify the magnitude of ERN, indicating that people's neural response to errors is heightened, thereby resulting in higher levels of anxiety. However, stress may reduce the magnitude of RewP, indicating a decrease in reward sensitivity and potentially increasing the susceptibility to depression. In summary, this article offers insights on how to articulate the connections among stress, anxiety, depression, and related factors. Furthermore, this article introduces a novel perspective on approaches to treating and preventing anxiety and depression.

Keywords: Anxiety, Depression, Error-Related Negativity, Reward Positivity.

1. Introduction

Anxiety and depression, as their diagnoses are increasing, have risen to be a global public health issue, particularly in the face of stress factors. Data released by the WTO reveals a significant rise in anxiety and depression-afflicted people because of COVID-19. The phenomenon of anxiety disorders and major depressive disorder witnessed a surge of 26% and 28%, respectively [1], making it a priority to understand the relations among stress, anxiety and depression, and related prevention and control methods and treatments.

This paper has taken the neural responses to error and reward as a starting point. These neural responses exert a profound influence on individual emotions and behavior [2]. It should be noted that these neural responses can experience changes in stressful situations so as to affect the anxiety and depression of an individual [3]. This theoretical foundation has found support in several empirical studies. For instance, research has discovered that stressful events, like corporal punishment, can amplify neural responses to errors while decreasing those to rewards, thus leading to a higher risk of anxiety and depressive symptoms [4]. Similarly, Melton et al. (2019) conducted a study and found that

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stressful events, including corporal punishment, are likely to increase neural responses to errors and diminish neural responses to rewards, thereby giving rise to a greater risk of anxiety and depressive symptoms [5].

The paper will explore the impact of stress on neural responses to errors and rewards and how this, in turn, affects anxiety and depression. Several studies have shed light on this intricate mechanism [6]. Looking into these connections, it is hoped that the article can improve an understanding of the neurobiological mechanisms of anxiety and depression and provide some valuable insights into more effective prevention and treatment strategies.

2. Error-anxiety

Prior to describing details about how the neural response to error influences anxiety, it is important to introduce a major concept known as Error-Related Negativity (ERN). ERN refers to an electrical activity observed in the brain when mistakes are made. It is generated in the prefrontal central sulcus region of the brain, a brain area that is associated with decision-making and error monitoring. ERN is regarded as the brain's immediate response to errors that reflect cognitive and emotional reactions to them [7, 8]. Existing research has used ERN to study different kinds of psychological disorders, especially anxiety disorders.

The findings of the study reveal that ERN may function as a biomarker for anxiety symptoms, indicating an important connection between ERN and anxiety. To be specific, a strong association exists between ERN and various types of anxiety disorders, such as GAD generalized anxiety, and SAD social anxiety disorder, suggesting a stronger neurological response to errors between them. [7]. Since anxiety and depression often concur, clinical diagnosis becomes somewhat difficult. However, as shown by research, ERN can make a clear distinction between the two conditions. For example, in a review article published in 2016, Dr. Meyer noted that the ERN was able to distinguish between highly co-morbid clinical diagnoses (e.g. anxiety and depression) and was associated with specific cross-diagnostic and clinically relevant phenotypes (i.e. examining symptoms). The article also states that the ERN shows excellent psychometric properties and is able to predict a large amount of variance in clinical outcomes [8].

In the 2012 study by Weinberg A et al., they found greater ERNs and increased differences between incorrect and correct trials in patients with GAD, and this enhancement was not seen in patients with GAD and MDD co-morbidities, suggesting that co-morbid depression may moderate the relationship between ERN and anxiety [9]. In addition, the magnitude of the error-related negative wave (ERN) is associated with both specific anxiety-related processes and depression, but in opposite directions [10]. All the studies point to the possibility that ERN may be associated with certain forms of anxiety and related traits [11]. The reason why the ERN shows a strong correlation with anxiety may be due to the fact that the brains of people with anxiety disorders may respond more strongly to errors. For example Moser, J. S. et al. found in a study that anxiety was associated with enhanced error detection, as reflected by an increase in ERN amplitude [12].

The biological mechanism behind this appears to be related to the anterior cingulate cortex (ACC), which has been shown to be involved in ERN production. More specifically, the dorsal part of the ACC (dACC) or the middle cingulate cortex appears to be particularly important for ERN production [13, 14]. There is also a cloud analysis of anxiety disorders that shows reduced grey matter volume in the right anterior cingulate cortex (ACG) in patients with anxiety disorders [15].

Stress plays a significant role in modulating ERN and subsequently influencing anxiety [16]. Stress can be defined as a state of threatened homeostasis provoked by a psychological, environmental, or physiological stressor [17]. Acute and chronic stressors have been found to significantly impact the ERN magnitude, highlighting the malleability of ERN in response to environmental demands [16]. Research has found that stress exposure enhances the amplitude of ERN, indicating an increased neural response to errors [18]. This is consistent with the general understanding that stress heightens our attention to potential threats and mistakes, which can lead to heightened anxiety levels. Especially, stressful individuals with higher ERN are more susceptible to symptoms related to anxiety disorders, indicating

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that the neural mechanism underlying error sensitivity may act as a potential pathway for stress in increase anxiety [19]. Notably, the effects of stress on ERN and anxiety might be subject to various factors like resilience, coping strategies, and the nature and duration of the stressor [18]. For this reason, an understanding of the relationship among stress, ERN, and anxiety is conducive to effective interventions and treatments for anxiety disorders [18].

3. Reward-depression

Similar to ERN, Reward Positivity (RewP) functions significantly in depression-related studies. RewP, a neurophysiological response, occurs about 300 milliseconds after the presentation of a reward or a positive outcome. It manifests itself as a positive deflection in the EEG signal and is generally larger for rewards than for non-rewards [20]. This neural response is believed to intensify the sensitivity of the brain to rewards and its capacity to learn from positive outcomes.

The relations between RewP and depression have been extensive studied. As indicated by several studies, depressed individuals with lower RewP amplitude suggest a decreased sensitivity to reward [21], What's more, RewP amplitudes desmonstrate a negative correlation with the severity of depressive symptoms [22]. These findings can further prove a strong association between RewP and depression.

According to research, individuals with depression, or at risk for depression, often exhibit a diminished RewP, indicating a decreased neural response to rewards [20, 23]. It is believed that the reduced reward sensitivity contributes to anhedonia, which involves s lack of pleasure or interest in enjoyable activities and is a common symptom of depression. Furthermore, it is found that lower RewP can serve as a predictive factor for the future onset of depressive symptoms, suggesting its potential to be a biomarker for depression risk assessment [23].

It seems that stress plays an important role throughout the process. Research has found that stress experiences can reduce RewP, suggesting a potential to lower reward sensitivity and increase depression risk, which aligns with the broader body of literature that shows stress exerts a certain impact on depression [24, 25].

Furthermore, chronic stress may lead to long-term changes in the brain's reward system, which may contribute to the persistence of depressive symptoms [26]. Furthermore, there is also evidence that triggers such as chronic stress lead to changes in functional links within the brain's reward areas, which in animal models modulate reward-related depressive behaviours and symptoms, including socialization (social avoidance and anhedonia) [27].

Like ERN, RewP is also thought to be generated in the anterior cingulate cortex (ACC), specifically in the ventral part of the ACC (vACC). The vACC is involved in processing rewards and other positive stimuli, and alterations in its activity have been linked to depression and anhedonia [28]. Structural abnormalities in the ACC, including reduced gray matter volume, have been found in patients with depression, further supporting the role of this region in depression [29].

4. Future directions

Previous sections have discussed the relationship between neural responses to errors and rewards and anxiety and depression and their biological mechanisms, and have also briefly described the effects of stress on ERN and RewP. In terms of future research, there are several important avenues to further investigate these complex relationships and inform preventive interventions for the treatment of anxiety and depression.

Regarding stress as a neurobiological mechanism that influences neural responses to error and reward and how it further influences depression and anxiety, although we have identified the anterior cingulate cortex (ACC) as a key region involved in the production of ERN and RewP, the specific neurobiological mechanisms underpinning these processes are still poorly investigated [30].

Future research could use neuroimaging methods such as functional magnetic resonance imaging (fMRI) or positron emission tomography (PET) to identify the neural circuits and neurotransmitter systems involved in ERN and RewP production to examine in more detail how neural responses to errors

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and rewards under stressful conditions affect anxiety and depression. Future research can conduct an investigation into the potential other brain regions and networks to modulate these neural responses.

As for interventions, it is possible to develop cognitive behavioural therapies to specifically cope with poor neural responses to errors and rewards. Neurofeedback enables individuals to learn brain activity regulation and can reduce ERN or increase RewP [31].

To conclude, a better understanding of the complex relations between stress, anxiety, and depression serves as an insight into the prevention and treatment strategies for depression and anxiety disorders.

5. Conclusion

This paper explores the influence of stressful situations on anxiety and depression and their mediation effect on neural responses to errors and rewards. The paper focuses on the neural responses to ERN and RewP and their impact on anxiety and depression. The findings indicate an important role for ERN and RewP in anxiety and depression, particularly in the context of stress. It is also suggested that these neural responses can be changed to further influence anxiety and depression in an individual. Regarding neurobiological mechanisms, it has been identified that the ACC serves as a major region for ERN and RewP production.

This paper also investigates the influence of stress on the ERN and RewP and their potential subsequent impact on anxiety and depression. It is found that stress can augment ERN, indicating an increased neural response to errors. The increased response can cause higher levels of anxiety. Meanwhile, it is observed that stress can also lower the size of the RewP, infdicating reduced reward sensitivity, which has the potential to increase depression risks. The paper offers new insights into the prevention and treatment strategies for anxiety and depression.

Despite the insights, this paper is not without its limitations. The paper lacks a detailed discussion of the specific neurobiological mechanisms. Besides, neuroimaging methods such as fMRI or PET could be used in future studies for further investigation into the influence of neural responses to errors and rewards under stressful conditions on anxiety and depression.

In conclusion, a better understanding of the complex relations among stress, anxiety, and depression can contribute to future research on effective prevention and treatment strategies for depression and anxiety.

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