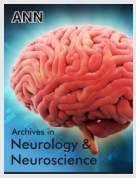

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Mini Review

The Role of Monoamine System in Core Affects and Basic Emotions

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Abstract

Affective disorders are a leading cause of disability worldwide, and drugs targeting monoamine neuromodulators are considered to be the first choice of treatment for these diseases. Here, we further explore the relationship between the monoamine neuromodulators with the core affects or basic emotions and try to give a very simple model for basic emotions: three primary color model. In this model, we try to put the 3 monoamines together with the core affects or basic emotions in a plane, like the three-primary color: DA-reward (joy), NE- stress (fear and anger), and serotonin- punishment (sad). This model can be helpful to better understand the dynamics of basic emotions, the etiology of affective disorders such as depression, and the actions of respective psychoactive drugs.

Keywords: Basic emotions; Monoamine; Core affect; Dopamine; Norepinephrine; Serotonin; Stress; Reward; Punishment

Introduction

Affective disorders, such as depression, have been identified as a leading cause of disability worldwide [1]. However, the treatments are not as good as expected, because of lacking knowledge about neural basis for emotions. Studies of the neural basis of emotion have a long history within neuroscience and are still an active field of experimental and theoretical research [2]. Most of the work focuses on identifying neural structures responsible for emotions. This work culminated in the invention of limbic system theory of emotion around mid-19th century. However, this work was frustrated by fMRI studies which want to find a specific locus for a specific basic emotion [3-5].

Anyway, there is one thing that has been proved to be right is the monoamine basis for emotions. Monoamine (including serotonin, noradrenaline and dopamine) has been showed to be the substrate for emotion ever since the 50s-60s in last century [6]. So far, most the antidepressant and anti-psychotic drugs are targeting the monoamine system, and dysfunctions of the monoamine system have been proved to be involved in many mental disorders such as depression [1,7-9], anxiety [10], post-traumatic disorders [11], and attention-deficit hyperactivity disorder [12-14]. The monoamine producing systems originate from three most concentrated neuclei (locus coeruleus- norepinephrine; raphe nucleus- serotonin, ventral tegmental area-dopamine), and project their axons and release these neuromodulators diffusely and widely throughout the cerebral cortex [15]. These properties fit perfectly with one property of emotion: "all or none" properties for an emotion. This means if you are happy, the whole brain will be happy; if you are angry, the whole brain will be angry. So, it might be nonsense trying to find one specific locus in the brain for one basic emotion.

However, even though many studies from different research field support the idea that monoamines are the substrate for emotions [16], their effects are still quite mixed. For example, antidepressant drugs affect almost all the monoamine neuromodulators and are also used for almost all affective diseases such as anxiety, phobia, depression et. al [17]. There is a need to improve the

conceptualization and classification of the emotional states and the monoamine neuromodulators. Here we review some experimental papers about their difference in modulating emotions and try to differentiate their functions in controlling emotion and behavior. In addition, we will introduce a new hypothesis about monoamine with core affects: three monoamine neuromodulators underlie the 3 core affects (dopamine-reward, serotonin-punishment, norepinephrine-stress), and they work together to make different basic emotions, like the three primary colors. The dopamine system has been proved to be involved in reward [18-20], the noradrenaline has been related to the "fight or flight" responses at stressful events [21,22], and the serotonin system seems to be related to punishment [23].

The Monoamine System and Core Affects

Norepinephrine–stress

The brain norepinephrine system is well known to be activated by acute stress [1,24,25]. The stress is any threat, either real or perceived, to the organism, which would induce robust NE release. Following exposure to a stressor, norepinephrine is released from the LC to almost all the brain cortex and other limbic areas, such as hypothalamus, which was prompted to release corticotropin releasing hormone to activate the HPA axis (hypothalamus-pituary-adrenaline axis) [24,26-28], where more norepinephrine/epinephrine is released from the sympathetic system to the blood. Even though the LC is very small, the axons of these neurons project to essentially the whole brain, and potentially influence the entire nervous system [29,30]. The robust norepinephrine release will lead the animal to certain kind of active behavior: "fight or flight" [24,31,32]. In the periphery autonomous nervous system, NE acts as a sympathetic neurotransmitter, together with adrenaline, acts as stress hormones, directly increases heart rate, triggers the release of glucose, and increases blood flow to skeletal muscles, to be ready for "fight-or-flight" responses [8,19,33-39], or "fear and anger emotions [24,37,40,41].

Dopamine – reward

Ever since Wise (1980) proposed the hedonic hypothesis of dopamine, mesolimbic dopamine in the brain has long been linked to the rewarding processes in almost all the animal kingdom [42-46] and proposed that dopamine is a signal of stimulus salience, providing feeling of enjoyment. From then on, lots of papers have confirmed dopamine's role in the rewarding signals [47-53]. For example, many studies on intracranial self-stimulation have established the important role of the dopamine system in reward behavior [51,54-56]. In addition, drug addictions have been proved to be involved in the reward system by affecting dopamine release, reuptake inhibition [20,45,57-60]. Together, these studies suggest an involvement of dopamine neurotransmission in the acute and long-term rewarding system [58,61-63].

Serotonin – punishment

Serotonin plays a critical role in a wealth of psychiatric conditions, such as depression, manic anxiety and obsessive compulsions [64-66]. However, despite the importance of serotonergic pharmacotherapies, its roles in normal emotion are still mysterious [66]. Its major function can be divided into three aspects: 1) serotonin is involved in prediction of aversive events [23,67]; 2) it is involved in behavioral inhibition, preventing ongoing action in light of prediction of aversive outcomes [68]; 3) it is involved in the treatment of depression [66]. These functions are rather complicated and seem contradict to each other [69,70]. More than 20 years ago, Deakin and Graeff hypothesized that some serotonin pathways are involved in response to aversive stimuli [23,66], and dysfunction of these pathways contributes to the pathophysiology of anxiety and affective disorders [69,71]. And later many more studies have related serotonin to punishment, for example, Robinson shows that "serotonin is critical for punishment-induced inhibition" [72] and Dayan concluded that: "At a global level, serotonin is richly involved in the behavioral neuroscience of punishment and threat" [66,70].

Monoamine and Basic Emotions

The stress, reward and punishment are the core features of emotions, or core affects. Core affects are not emotions by themselves [73], instead they are just three characteristics of emotions. These three core characterizations constitute four basic emotions: fear and anger, joy, sadness (Figure 1) [16,34,74]. The three core affects are also related to three kinds of behaviors: stress-"fight or flight", reward- "relax and enjoy", punishment- "freeze and inhibition" [1] (Figure 1).

Figure 1: Three Primary Color model of basic emotions. Stress, reward and punishment are the core features of emotions, called core affects, and three monoamines are related to three core characteristics of emotion: norepinephrine-stress, dopamine-reward, serotonin for punishment. These three core characterizations constitute the three basic emotions: fear-anger, joy, sad. For fear and anger share too many similarities, they are classified as one basic emotion: the stressful emotion. The three core affects are also related to three kinds of behaviors: stress-fight or flight, reward- relax and enjoy, punishment-freeze and inhibit, modified from our previous publications.

Stress results from threat to the homeostasis and wellbeing of the human being8, and it is due to uncertainty about the situation

[8]. Stress can activate the NE/LC system, which induces "fight or flight" behaviors, and "fear and anger" emotions [75]. It seems that stress first induce fear due to the first appraisal, then anger with the secondary appraisal [76]. Fear is associated with appraisals of uncertainty and induce avoidance; while anger is associated with certainty and induce approaching [37]. According to Lazarus's reappraisal theory, after the second appraisal, an individual employs a positive reappraisal (happy, or rewarding emotions will be induced) and negative reappraisal (sad, or punishing emotions will be induced) [77,78]. The emotion joy is due to positive reappraisal: coping successfully, this is really the case for dopamine neurons [61,79,80], dopamine can be released by successfully removing the stress, or coping successfully with the stressful situation [79,81]. Therefore, dopamine release is not determined by rewarding stimuli or aversive stimuli, it is determined by if the coping process is successful or not [55,79]. We might also extend this process to the emotion joy or happy: the happy emotion is due to successfully coping with the situation, which can induce relaxation and enjoyment.

At stressful event or traumatic event, people might experience negative reappraisal [82], which is due to coping failure. Therefore, emotion sadness is due to negative reappraisal: coping failure. Like dopamine's role in reward prediction error, and the role of aversion prediction error was also proposed for serotonin [83]. Therefore, serotonin is due to coping failure, and we might also extend this definition to the emotion sad. Serotonin is correlate positively with aversion and negatively with reward [66]. Serotonin has a major behavioral effect is suppression or inhibition or freezing, or the behavior resulted from sad emotion is relaxation and enjoyment. This is a kind of passive avoidance by not doing actions at punishment, which is different from active avoidance of fight and flight induced by norepinephrine [84].

Conclusion

This paper presents a new model for monoamine neuromodulators and basic emotions, like primary colors: red-NE-stress-fear/anger, green-reward-joy, blue-punishment-sadness. Many papers have linked the monoamine neuromodulators to basic emotions, such as the "new three-dimension model" [15], which arranged the basic emotions in a three-dimensional equation. Here, we further explore the relationship between the monoamine neuromodulators with the basic emotions and get an even simpler model: three primary color model. In this model, we try to put the 3 monoamine neuromodulators in a plane: dopamine-joy-green, norepinephrine-surprise-red and serotonin-dislike-blue (Figure 1). This model is very simple, and it will be very helpful to better understand the dynamics of basic emotions, the etiology of affective disorders such as depression, and the actions of respective psychoactive drugs.

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Competing Financial Interest

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