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Chapter 11

The Role of Serotonin in Aggression and Impulsiveness

Fatih Hilmi Çetin, Yasemin Taş Torun and
Esra Güney

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Abstract

Serotonin is a neuromodulator that has a critical role on the regulation of essential events in neuronal and glial development, such as cell proliferation, differentiation, migration, apoptosis, and synaptogenesis, and acts as a developmental signal. It has been known that a serotonergic system is associated with many psychiatric disorders. The serotonergic system also predominates on the etiopathogenesis of two important endophenotypes: impulsivity and aggression. Impulsiveness is defined as personality trait and an implusive temperament is associated with clinical conditions such as pathological gambling, eating disorders, and borderline personality disorder as well as being a risk factor for self-harm, suicide, and emotional liability. Aggression is not a personality trait like impulsivity, but it is the behavior of harm or injury to others. Besides being a natural human behavior toward survival, aggression can be harmful to the individual and the community when it is constant and excessive. In this chapter, we aimed to review the role of the serotonergic system on impulsivity and aggression, which are two important endophenotypes that identified in many psychiatric disorders.

Keywords: serotonin, aggression, impulsivity, impulsive aggression, psychiatric disorders

1. Introduction

Serotonin is a neuromodulator that acts as a developmental signal [1]. The serotonin is formed by decarboxylation of the 5-hydroxy-tripotafan that synthesized from tryptophan via the tryptophan hydroxylase enzyme [1]. Serotonin has a critical role on the regulation of essential events in neuronal and glial development, such as cell proliferation, differentiation, migration, apoptosis, and synaptogenesis [2]. Because of this broad spectrum of serotonin functions, pathologies in serotonergic system have been held to account on many psychiatric

disorders such as mood disorders, anxiety disorders, attention-deficit hyperactivity disorder (ADHD), and autism spectrum disorders (ASDs) [3]. Consider of heterogeneous clinic and different symptom clusters of psychiatric disorders, the serotonergic system predominates on the etiopathogenesis of two important endophenotypes: impulsivity and aggression [4, 5]. Impulsiveness is defined as personality trait, which is a multidimensionality [6]. An implusive temperament is associated with clinical conditions, such as pathological gambling, eating disorders, and borderline personality disorder as well as being a risk factor for self-harm, suicide, and emotional liability [3, 7]. Brain imaging and pharmacogenetic studies have demonstrated that serotonin dysfunction is associated with impulsive behaviors [8]. Aggression is not a personality trait like impulsivity, but it is the behavior of harm or injury to others [9]. It is harmful to the individual and the community when it is constant and excessive, besides being a natural human behavior toward survival [9]. Three types of aggression have been defined as psychotic, impulsive, and proactive [4]. The serotonergic system is associated with impulsive aggression which is manifested by provocation rather than proactive aggression which is goal-oriented and planned [4]. Nowadays, researchers are directed to endophenotypes in psychiatric diseases with heterogeneous clinic in order to develop new treatment methods and to elucidate etiopathogenesis. In this chapter, we aimed to review the role of the serotonergic system on impulsivity and aggression, which are two important endophenotypes that identified in many psychiatric disorders.

2. Impulsivity

Impulsivity is defined as the tendency to exhibit behavior without adequate mental assessment of possible outcomes [10, 11]. From this point of view, it can be said that impulsive dimension can be mentioned in the process of thought up to behavior [12]. In this dimension, there have been different definitions such as impulsive choice, impulsive reflection, and impulsive action that can be measured by different assessment tools that have subjective or objective qualities [10, 13, 14]. Impulsive choice described as prefer less valuable prize in soon afterwards rather than the more valuable prize in the distant future, the inability of the individual to gather adequate data on the risks describes as impulsive reflection and a lack of motor inhibition described as impulsive action [15]. The lowa gambling test provides data about impulsive choice known as delay-discounting [16]. Stop-signal reaction time and go/no go tasks are objective assessment methods that assess motor inhibition. In these tasks, individuals should wait until the appropriate signal arrives and stop the movement when no go or stop signal is received. “Waiting impulsivity” described as the failure to start the movement and “stopping impulsivity” described as the failure to stop or restrict the movement. The Barratt impulsivity scale and impulsive behavior scale are subjective self-report scales, each with different subscales and provide data on different dimensions of the impulsivity [10, 12, 13, 15, 17–19].

The main pathophysiological mechanism is the disruption of reciprocal equilibrium in corticostriatal cycles [10]. Impulsive behaviors come out as a result of impaired inhibitor function of the prefrontal cortex (PFC) to delay the award and stopping or restricting the behavior,

additionally increased striatal output to achieve a small and certain but definite near future reward rather than the far-future reward, with a high value but a low degree of uncertainty [10, 13, 15].

Recent studies showed that the basic region that rejects the award postponement when the award is quick earning despite small was nucleus accumbens; contrary the basic region that provides inhibition is the orbitofrontal cortex [20, 21]. Anterior cingulate cortex and right inferior frontal gyrus are two other important regions for inhibition [22, 23]. Nucleus accumbens is also associated with impulsive cycle inflicting from the striatum, also accompanied by amygdala and hippocampus [24]. This network includes dopaminergic, noradrenergic, and serotonergic neurotransmission.

Increased impulsiveness is associated with many psychiatric disorders, although healthy individuals have a personality trait and an advantage in situations where the organism needs to move quickly [10]. ADHD, substance abuse, eating disorders, bipolar disorder, behavioral addictions, and borderline/antisocial personality disorders are typical psychopathologies associated with impulsivity [25]. In these disorders, impulsive behavior patterns can be described in many expressions; but aggression is the most accentuated and evidence-based one.

3. Aggression

Aggression is the pattern of behavior that an individual exhibits in such a way as to damage himself or environment [4]. Natively, aggression is necessary to survive. For example, to protect ourselves and our beloved ones from danger, to supply the food and water for survive, and to react to possible risks of the organism on threat [26]. Investigating aggressive behaviors by subcategories is beneficial both in clarifying etiopathogenesis and in adjusting the treatment process. In previous papers, aggression had been categorized as offensive and defensive such as a dangerous or evasive response to a sense of fear, the most frequently preferred classification in the recent literature categorized into three groups: impulsive, proactive (also known as organized, instrumental, or predatory), and psychotic. Impulsive aggression (54%) is the most common category followed by proactive aggression (29%), and psychotic aggression (17%) [27, 28]. As predicted, psychotic aggression is a process related to positive symptoms of psychosis, such as hallucinations or delusional content. In proactive aggression, the individual exhibits this behavior in a planned manner to achieve a blazing benefit such as money or revenge. Impulsive aggression is a behavioral pattern which is accompanied by physical symptoms after stimulation of the sympathetic system, often associated with feelings of fear, inhibition, or anger, which are manifested by stress, threat, or provocation [28].

The main pathophysiological mechanism of impulsive aggression is the altered balance—to the detriment of prefrontal cortex—between the inhibitor stimulants from cortex to subcortex/limbic system and excitator stimulant as strong tendency to realizing behavior from cortex [4]. PFC dysfunction results in inadequate risk assessment and top-down inhibition is reduced [4, 27]. Bottom up outputs that have increased frequency and amplitude especially from the amygdala toward the orbitofrontal cortex contribute to impulsive aggression [27, 29]. In many human and

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