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Serotonin and Emotional Decision-Making

Sara Puig Pérez

Abstract

Serotonin is one of the most important neurotransmitters involved in emotional regulation, which affect decision-making. In fact, specific genes regulate the transporter protein of serotonin, making people prone to show or not higher amygdala activation. Higher activation of specific components of the limbic system, such as amygdala, results in a higher susceptibility to make decision taking into account the environmental and emotional aspects and not only rational elaborations of the facts. It makes the response of decision-making more visceral or emotional in contrast to people with lower amygdala activation. Therefore, the importance of serotonin regulations impacts on daily and important decisions.

Keywords: serotonin, amygdala, decision-making, behavior

1. Introduction

Nowadays, decision-making has been considered as one of the most complex cognitive functions that use other superior processes such as learning, memory, and feedback sensibility [1]. Theoretically, when people have to make a decision, they are placed on a continuum of uncertainty being “complete ignorance” one pole and “certainty” the other one [2]. In this case, there are difficulties to identify the level of uncertainty (ambiguity), it could be impossible to determine the probability of gain or loss, regardless of the fact that consequences are established and clearly known. In contrast, in those situations where there is risk of uncertainty, although the consequences are stable and clearly known too, gain of fail result can be calculated. So, accordingly, decisions can be made considering as key construct the range of ambiguity or risk of uncertainty [2, 3].

The cognitive-experiential theory supported by Epstein’s group [4] distinguishes between two qualitative systems of information processing in decision-making: the rational and the experiential system. The rational style of thinking is characterized by a free emotional perspective, which results in a more analytic, conscious, and effortful process. In contrast, the experiential system is based on emotions, being more automatic, effortless, imaginative, and unconscious (Epstein, 2010). Interestingly, the way people process the inputs from the environment and make decisions is considered in two ways: analytical and intuitive [5]. So, the thinking styles and the decision-making styles probably share an important background. But, decision-making is considered independently from emotional processes and brain neurochemical balance. In this chapter, we will summarize the physiological overlapping between emotional and decision-making processes and the effect of serotonin neurotransmitter on the modulation of these cognitive functions.

2. Main brain regions involved in emotions and decision-making

The main brain structure involved in decision-making is the prefrontal cortex (PFC), which is considered nowadays as the main location of executing cognitive functions. In fact, it has been considered the PFC as the central key structure for cognitive functions as attention for relevant environmental stimuli, objective selection, cognitive control, planning, and monitoring performance [6, 7]. For goal-directed behavior [8] and attention [9–11], subcortical and thalamic regions are involved together with the PFC leading to a complex top-down cognitive control network. In this line, behaviors controlled by other subcortical or cortical areas out of PFC control network become habits or inflexible behaviors, mostly dependent on simple sensory motor associations [12].

It is important to take into account that the PFC region is controlled by subcortical regions involved in emotional processing such as amygdala or nucleus accumbens (NAc) [13, 14]. Both are considered key structures in processing the signal of the environmental stimuli, taking into account the emotional valence, in order to classify them as appetitive or aversive [15–17]. At the same time, PFC is connected with the orbitofrontal cortex (OFC) in voluntary choices and to the anterior cingulate cortex (ACC) in monitoring the outcome of our choices [18, 19]. These connections support the well-known effect of emotions on decision-making. In fact, lesion model studies performed with rats and nonhuman primates showed that NAc injury affects negatively response inhibition and cognitive flexibility [20–22]; meanwhile, amygdala inactivation or lesion affects the selection of relevant information, which is needed in situations with emotional value to coordinate cognitive, physiological, and behavioral responses [17, 23, 24].

Interestingly, although the dorsolateral prefrontal cortex (DLPFC) has been considered as the cognitive brain region per excellence [25, 26], there is growing evidence suggesting that DLPFC plays an important role in emotional regulation and motivated behavior [27–32].

3. Physiological overlapping between emotions and decision-making

When someone has to choose between doing something or not, he balances the immediate reward of doing it as well as the risk of incurring future negative consequences. This fact is known as the concept of willpower, which involves two brain systems' activation: the impulsive system and the reflective system [33] (see **Figure 1**). According to that, the decision-making process will mainly depend on neural substrates, which are affected by emotions because of the modulation that feelings make on neurotransmitter systems.

Main structures involved in the impulsive system are amygdala and striatum [33], which are the structures involved in short lived and very quick responses [34]. As we explained above, amygdala is responsible for attributing affective or emotional value to stimuli perceived evoked through hypothalamus and autonomic brainstem nuclei, which produce changes in internal milieu and visceral structures (e.g., *striatum* and periaqueductal gray) [35]. Amygdala plays a role in emotional decision-making, even in stimuli with an affective value learned by experience (e.g., money or drugs). It has been shown that autonomic response to the gain or loss of important amounts of money depends on the amygdala integrity [1]. In the same line, in addicts, it has been show an exacerbated autonomic response similar to monetary gains [36], which could be related to abnormal activity in the amygdala-ventral striatum system that probably would result in a heightened reward perception of the stimuli [37].

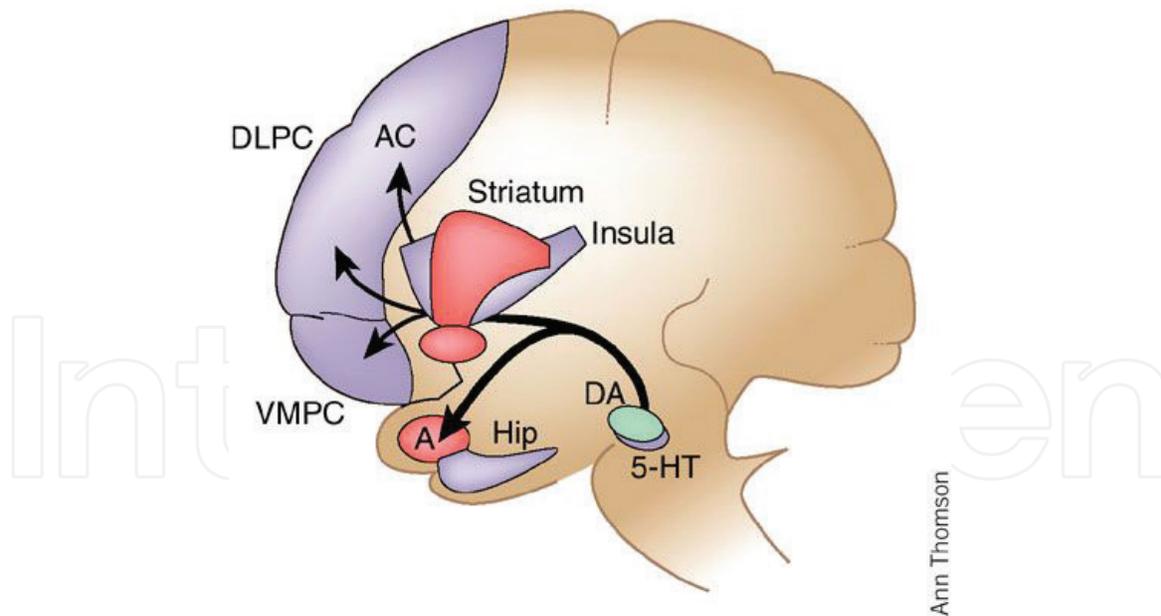


Figure 1. Diagram from key structures involved in the impulsive (red) and reflective system (blue). A: amygdala, VMPC: ventromedial prefrontal cortex, AC: anterior cingulate, DLPC: dorsolateral prefrontal cortex, hip: hippocampus, DA: dopamine, and 5-HT: serotonin. Extracted from Ref. [33].

In contrast, the reflective system involves hippocampus, insula, AC, and PFC structures (ventromedial prefrontal cortex—VMPC, lateral orbitofrontal, inferior frontal gyrus, and DLPFC) [33]. The VMPC is crucial to induce affective states from recall to imagination, because it is responsible to reactivate the pattern of the affective state experienced in the past of reward or punishment that was developed from the brainstem nuclei [35] and to which the brain preserves the neural pattern [1]. In fact, patients with damage or people with functional abnormalities in VMPC [1] (Erns and Paulus, 2005) show impairments in decision-making. However, the normal function of the VMPC depends on the integrity of other neural systems. The insula, hippocampus, DLPFC, and somatosensory cortices need to be preserved for representing patterns of emotional or affective states and memory, but they need to preserve their integrity for the correct functioning of the VMPC too. Impairments in decision-making in patients with right parietal damage [1] and in people with functional abnormalities (Erns and Paulus, 2005), including the insula and somatosensory cortex, have been observed. Same difficulties in decision-making have been observed in patients with damage on DLPFC (Clark, Cools and Robbins, 2004). For these reasons, it can be concluded that the decision-making process depends directly on the correct functioning of other brain systems involved in memory and emotional regulation [33]. This neural overlapping suggests a functional interconnection between memory, emotions, and decision-making cognitive processes, being all connections between these brain systems are located in VMPC [1] (Clark et al., 2004).

In line with those exposed above, Rolls [38] highlights the importance of emotions in decision-making processes giving the fact that the resulting behavior of a decision is the consequence of two brain systems (see **Figure 2**). On the one hand, the emotional system is responsible for the behavior directed to reward or avoidance of punishment in terms of aptitude to natural selection [39–41]. OFC and amygdala have been related to the reward process [39], giving a reward/affective value of the stimulus processed firstly by sensorial main structures (see **Figure 2**). In contrast, the cognitive system depends on the frontoparietal network and responds to declarative knowledge and explicit goals [38]. The main contribution of Rolls [38, 39] was the establishment of the role of lateral PFC, which is considered the hub of modulation of emotion circuitry able to bias our behavior and conduct it agreeing to our explicit goals.

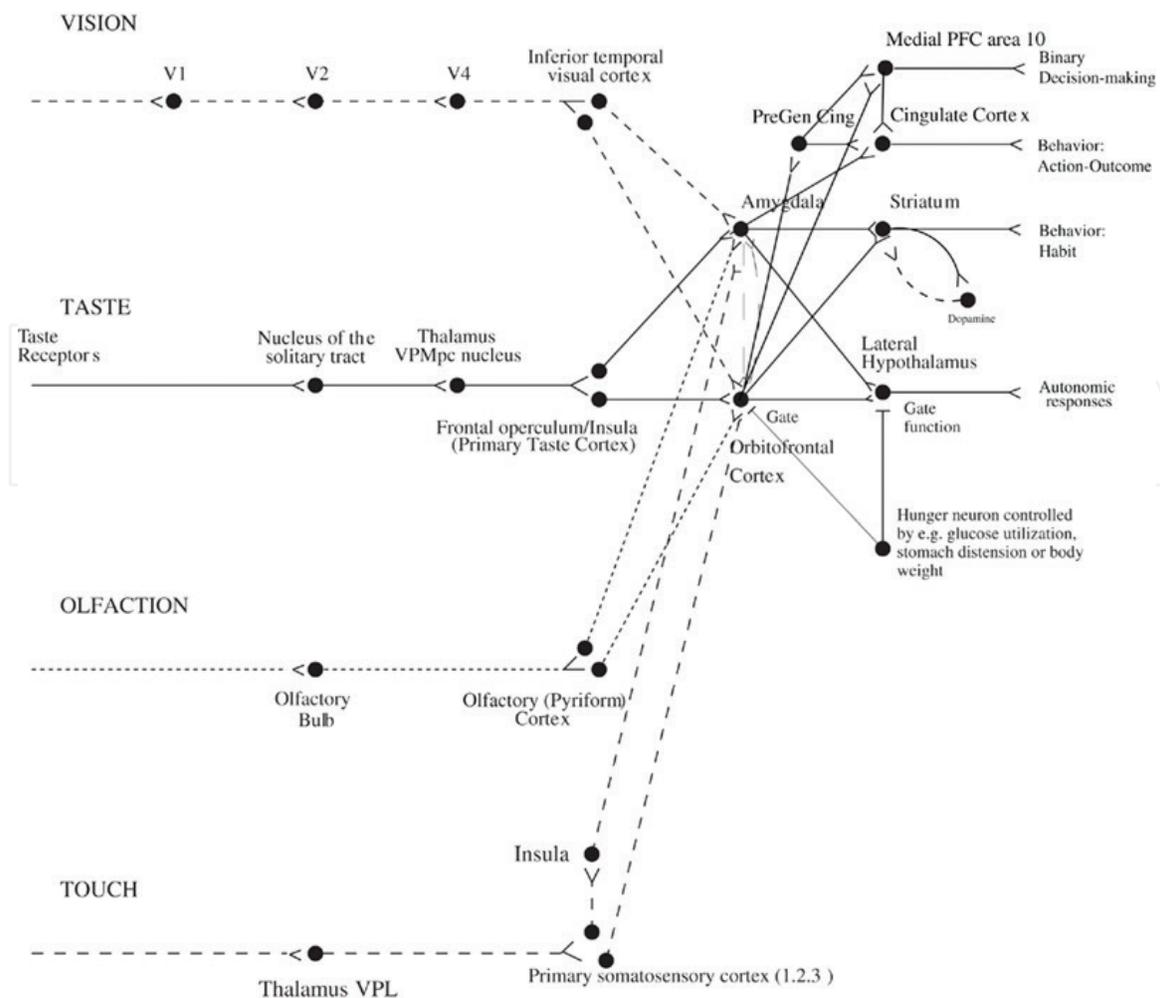


Figure 2.

Schematic diagram showing some of the connections of the taste, olfactory, somatosensory, and visual pathways in the brain. V1, primary visual (striate) cortex; V2 and V4, further cortical visual areas. PFC, prefrontal cortex. VPL, ventroposterolateral nucleus of the thalamus, which conveys somatosensory information to the primary somatosensory cortex (areas 1–3). VPMpc, ventro-postero-medial nucleus pars parvocellularis of the thalamus, which conveys the taste information to the primary taste cortex. Pregenual cingulate cortex. For the purpose of description, the stages can be described as Tier 1, representing what object is present independently of reward value; Tier 2 in which reward value is represented; and Tier 3 in which decisions between stimuli of different values are taken, and in which the value is interfaced to behavioral output systems. Extracted from Rolls [39].

4. Serotonin as key neurotransmitter in emotional decision-making

Why is serotonin the hub of decision-making? Considering the neural correlation explained above which regulates emotions and decision-making, the following question to consider is which neurotransmitter regulates these networks.

Neuroanatomical studies described the brain regions mainly regulated by serotonin. It has been stated that serotonergic neurons are located mainly in the brainstem raphe nuclei [42] and project to numerous cortical and subcortical regions. The innervation of serotonergic neuron from this area projects to the PFC, amygdala, and NA as well as to the ventral tegmental area (VTA), which have been related to reward processes, emotions, and decision-making [13, 14, 43]. Interestingly, the medial areas from PFC play a top-down regulation from these serotonergic regions acting as a self-feedback regulation mechanism [44]. But there is a big amount of brain regions sensible to the serotonin neurotransmitter, the effect of which depends on the receptor located in the region. Specifically, 5-HT_{1A} receptors are found mainly at hippocampus, hypothalamus, and septum

which are part of the brain networks suggested as part of the different ways of decision-making process [45]. In contrast, 5-HT_{1B} receptors are found mainly on deep subcortical structures as globus pallidus, substantia nigra, ventral pallidum, and dorsal subiculum [46, 47]. The 5-HT_{2A} receptors from medial PFC are located practically exclusively on dendrites of local neuron circuits and spines of pyramidal neurons [48]. Moreover, 5-HT_{2A} receptors can be found on amygdala, hippocampus, and frontal, piriform and entorhinal cortices, as it happens with 5-HT_{2C} [49]. Finally, 5-HT₆ receptors are mainly expressed on the cerebral cortex, NA, striatum, and hippocampus [50].

Apart from neuroanatomical evidence highlighting the sensitivity from brain structures related to emotional processing and decision-making processes, one of the most important evidence of the key role of serotonin in these processes is using drugs to regulate serotonin release [51]. For example, the use of serotonin reuptake inhibitors (SSRIs) is one of the most important antidepressants used in depression and obsessive compulsive disorder [52, 53]. Interestingly, there are evidence that SSRI treatment, being effective reducing depressive symptom, improves decision-making and the sensitivity to positive feedback [54]. In this line, serotonin helps to predict future punishment [55] and affects the process of positive stimuli [54]. Increasing serotonin levels can block the uptake of serotonin released in synaptic space using, for example, SSRIs. These drugs, applied acutely, increase serotonin concentration in terminal regions, as well as reduce serotonin concentrations in raphe nuclei due to the activate 5-HT_{1A} receptor [56, 57]. Although these drugs have been considered one of the most efficient ways to increase serotonin levels, it has been observed negative effects on brain development when they have been used in young individuals [58], and to several alterations of the balance of other neurotransmitter systems [59].

Interestingly, there is a big amount of studies interested on genetic basis of serotonin, mood disorders, and cognitive functioning. Along the different genetic studies done about serotonin, it can be highlighted the role of 5-HTTLPR s-allele, which has been strongly related to anxiety traits, poor SSRI treatment response and increase of prefrontal activity [60]. C(-1019)G 5-HT1A polymorphism increases the risk of depressive disorder as well as reduces the efficacy of SSRI drug treatment [61]. And in the case of G-697C, polymorphism from 5-HT_{2C} is related to suicide [62]. Regarding 5-HT_{3A} and 5-HT_{3B}, which show a large variety of polymorphisms, they have been related to major depressive disorder [63].

Regardless of the evidence showed till now, recent studies are still trying to clarify the role of serotonin in the decision-making process. In fact, decision-making should be considered as a complex sequence of different superior process, making difficult to deeply understand the role of serotonin in each phase of brain subtasks that involves the decision-making process. In fact, the main subprocesses of decision-making with serotonin that has been considered key moderator are reversal learning, attentional set shifting, reinforce devaluation, delay discounting, and response inhibition (see [51]). In fact, Homberg [51] concluded that serotonin acts as an integrating internal and external information, affecting cognitive functioning: when serotonin is high, there is a high vigilance behavior increasing therefore the top-down PFC control which leads to an improved reversal learning, attentional set shifting, and response inhibition meanwhile decreases delay discounting. In contrast, when serotonin is low, the top-down PFC is low too leading to an impaired reversal learning, reduced attentional set shifting as well as decreased response inhibition; meanwhile, delay discounting turns high. In conclusion, serotonin regulation affects brain region functioning involved in the subtask, which depends on the decision-making process.

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