MEMORY, DECISIONS AND EMOTIONS AFTER THE ADMINISTRATION OF COCAINE: ROLE OF DIFFERENT NEUROANATOMICAL STRUCTURES

MEMORIA, DECISIONES Y EMOCIONES TRAS EL CONSUMO DE COCAÍNA: EL PAPEL DE LAS DIFERENTES ESTRUCTURAS NEUROANATÓMICAS

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Abstract

Drug addiction is a serious mental illness characterized by the loss of control over the use of the substance, the compulsive search for the drug and the appearance of a negative emotional state when the substance is not present. Among all the substances of abuse, cocaine is among the most consumed in our country, with serious physiological, psychological and biological repercussions for its consumers. Thus, our goal is to describe and analyze different mental processes that may be influenced by the administration of cocaine, trying to assess whether its alteration is due to changes in anatomical structures responsible for mental, cognitive and emotional functioning. An exhaustive bibliographic search was carried out in the main scientific databases using the keywords exposed in the work. The consumption of cocaine induces alterations in the functioning of cerebral structures, among which the amygdala, prefrontal cortex and hippocampus stand out, with different consequences in the cognitive and emotional functions of the individual. The study of these mental processes and of the anatomical structures involved represents a great advance in the area of mental illness and cocaine addiction, providing knowledge for the progress of new possible therapeutic options.

Keywords: cocaine, drug addiction, cognition, brain structure.

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Resumen

La drogadicción constituye una enfermedad mental grave caracterizada por la pérdida de control sobre el uso de una sustancia, la búsqueda compulsiva de la droga y la aparición de un estado emocional negativo cuando esta no es suministrada. De entre todas las sustancias narcóticas, la cocaína está entre las más consumidas en nuestro país, con repercusiones de índole fisiológica, psicológica y biológica sobre la salud de los que la consumen. Por tanto, nuestro objetivo es describir y analizar los distintos procesos mentales que puedan estar influidos por el uso de cocaína, tratando de valorar si estas alteraciones se deben a cambios en estructuras anatómicas responsables de un buen funcionamiento mental, cognitivo y emocional. Con este fin, se llevó a cabo una búsqueda bibliográfica exhaustiva de las palabras clave aquí expuestas en las principales bases de datos científicas. El consumo de cocaína produce alteraciones en las estructuras cerebrales, entre las que destacan la amígdala, el córtex prefrontal y el hipocampo, con distintas consecuencias sobre el funcionamiento cognitivo y emocional del individuo. El estudio de estos procesos mentales y de las estructuras mentales relacionadas con ellos constituye un gran avance en el área de enfermedad mental y de la adicción a la cocaína, puesto que aporta conocimientos para el progreso de nuevas vías terapéuticas.

Palabras clave: cocaína, drogadicción, cognición, estructura cerebral.

Introduction

The National Institute of Abuse Drugs (NIDA) defines drug addiction as a chronic and recurrent mental illness, characterized by the loss of control over the use of substance, the compulsive search for it and the appearance of a negative emotional state when the drug is not present[1]. It is categorized within the DSM-V manual as a substance use disorder and is known to generate neuroadaptations in the brain as a consequence of consumption[2]. Cocaine is among the main drugs consumed in Spain, constituting a serious social problem in our country.

The number of cocaine users has increased, from approximately 14 million in 1998 to 18.8 million in 2014[3]. This prevalence can be different depending on two factors: age and sex. The prevalence according to age shows alarming data. In Europe 2.4 million people (1.9 % of young adults between 15-34 years) have used cocaine in the last year[4]. In addition, it is estimated that the average age of onset of consumption is around 21 years or even earlier (depending on the year analyzed), when the brain is still completing its ma-

turity. The survey on drug use in secondary education in Spain[5], where data is collected from 1994 to 2014 from a population between 14 and 18 years old, shows a prevalence of cocaine consumption of 3.5 % over any other drug consumption. Once in a lifetime, 1.8 % of consumption in the last month and 2.8 % of consumption in the last year. On the other hand, according to the indicator of hospital emergencies in consumers of psychoactive substances, cocaine remains the drug with the highest episodes of hospital related emergencies, located in 43 % of them, followed by alcohol.

Cocaine is a drug obtained from the leaves of the Erytroxylon Coca shrub, a plant native to the Andes and cultivated mainly in South America, in countries such as Bolivia, Peru and Colombia, although crops have also been found in Indonesia and Africa. The first publications that talk about cocaine were written by J. J von Tschudi in 1830, where he recounted its effects as a favorable drug referring to a decrease in the need of sleep and food intake. Later, in 1850, Paolo Mantegazza recommended the use of coca for nervous diseases, highlighting its euphoric effect. As we know it today, it was not until 1859 when the German scientist Albert Niemann isolated the alkaloid from the coca leaf. Between the years 1862 and 1865, Wilhem Lossen discovered his formula: C17H21O4N. From this moment on, cocaine began to be marketed as a remedy against sadness, nervousness, and turned into a prescribed drug for enhancing beauty, vitality and strengthening the vocal cords. The use of cocaine was extended among health agents because of its capabilities to penetrate the central nervous system (CNS) and its stimulating and pleasurable effects[6]. However, it was not until the late nineteenth century when doctors began to comment on the adverse effects of this drug.

Among the existing forms of cocaine, coca leaves, base paste or bazuco (unrefined cocaine sulfate) or cocaine base ("free base" or "crack") stand out, although the habitual consumption of cocaine is that of cocaine hydrochloride, normally snorted[7]. After its consumption sniffed, the speed of appearance of the effects is fast and its duration oscillates between 30-60 minutes. This form of abuse presents a relatively high absorption due to the intense vascularization present in the nasal mucosa[8].

Cocaine acts by intensively stimulating the CNS. In the short term, its consumption causes cognitive (feeling of increased attention and concentra-

tion, decreased mental fatigue, alertness, sensation of cognitive acuity, confusion...), behavioral and emotional (anxiety, euphoria, irritability, increase of speech...) and physical symptoms (insomnia, decreased appetite, arrhythmias, tachycardia, increased blood pressure, mydriasis...), as well as a pleasant and safety sensation[1]. In the long term, cocaine has serious consequences, known as it is as one of the most dependence producing narcotic substances[9,10], although neurological alterations, paranoia, alterations of mood, even hallucinations and psychoses have been also described[11,12].

With regards to its effects on the brain, the prolonged consumption of cocaine causes neurobiological alterations that modify the neurotransmission of dopamine, considered to be the main neurotransmitter involved in the reinforcing effects caused by the drug, together with noradrenaline and serotonin. It causes an excessive release of this neurotransmitter to the synaptic space and, at the same time, it blocks its reception, resulting in a cluster of dopamine located in the synaptic cleft and and a so derived pleasure sensation[13-15]. Thus, with prolonged exposure to cocaine the brain undergoes modifications, among which the adaptations of the reward circuit or reinforcement system stand out, which means the brain become less sensitive to natural stimuli.

This well-known brain reward system[16] is also activated by natural stimuli such as diet[17], sex[18] and personal relationships[19]. It is located in the limb-palestriatal area, formed by the ventral tegmental area (ATV), Nucleus Accumbens (NAc), pale ventral and prefrontal cortex (CPF)[20]. Generally speaking, it acts as a circuit in which the regions are interconnected by projections highlighting the existing communication between areas of the reward system and those related to emotions, memory or decision making, such as the amygdala, the hippocampus and the prefrontal cortex. The consumption of cocaine can alter the functioning of these structures and consequently modify our behavior, cognitive functions and emotional responses.

For all of these reasons, this paper analyzes the effects of cocaine use on these brain structures and their possible mental, cognitive and emotional repercussions, in order to advance in the knowledge of cocaine addiction and contribute to the development of new therapies and treatments for such mental illness.

Cocaine, amygdala and emotions

The amygdala is the brain structure which is responsible for providing emotional value to environmental stimuli and generating responses to them[21-23]. In addition to preparing the individual for fear stimuli, it plays a major role in the brain circuits involved in addiction[1]. The amygdala is composed of several regions or nuclei, but more particularly in addiction, the basolateral amygdala (BLA) has been implicated as a subregion of the amydala, having high influence on drug-related behaviors[24].

Different studies have shown brain neuroadaptations after cocaine consumption[25]. These alterations include, among others, an increase in cerebral blood flow in the limbic system, which is related to emotions[26]. Similarly, other studies report a hypersensitivity of this area to stimuli related to cocaine[27], which also suggests that emotional memories stored in the amygdala interfere with relapse[28] and persist for long periods of abstinence by becoming resistant to change (inflexibility)[29].

On the other hand, several neuroimaging studies on drug use have reported that the amygdala suffers hyperactivation in the presence of stimuli related to cocaine, which could explain the sensation of anxiety as experienced by individuals[30].

Cocaine, prefrontal cortex and decision making

Among the functions in which the CPF is involved there are: decision-making, attention, cognitive flexibility, analysis and planning[31]. Moreover, several studies with animal models conclude that the administration of cocaine causes alterations in the cognitive functions of the PFC, thus influencing the executive and decision making functions[32] among others[33-34]. On the other hand, studies with humans have used tests such as the task of the Iowa Gambling (IGT) or the task of predicting two options; there it is shown that cocaine users showed worse results in decision-making when faced with different tasks of choice[35].

As in the case of the amygdala, the PFC is divided into several areas, among which are the orbitofrontal cortex (COF) and the medial prefrontal cortex (mFPC). Several authors have proposed that dysfunction in the COF as a consequence of cocaine use, since it plays an important role in the development of addiction[36,37] and that the behavior, present in cocaine consumers, resembles that observed after COF injuries[38]. With neuroimaging studies in cocaine addicts, an alteration in the COF metabolism is shown, as well as an alteration of neuronal activity in the presence of stimuli related to the drug[37]. Additionally, the lower activity of COF is one of the reasons why subjects addicted to cocaine have alterations in cognitive tasks[39], while an alteration in the structural and functional plasticity in the mPFC after the consumption of cocaine has been demonstrated[40].

Cocaine, hippocampus and memory

The hippocampus is a decisive region in the acquisition of new knowledge and memory of different types[41]. Studies with animals show prove the administration of cocaine to cause alterations in hippocampal-dependent tasks, measured through the novel object test that evaluates explicit memory in rodents[42]. On the other hand, neuroimaging studies suggest an increase in hippocampal activation after cocaine consumption, which is a consequence of the neurotoxic effects thereof, as well as a decrease in glucose metabolism[30]. In addition, it has been shown that the deficits found in the hippocampus are related to alterations in the PFC and amygdale, for there is a connection between all the structures[43].

While this is true, the findings about the effects of cocaine on the hippocampus as found in the literature see to be contradictory. Deficits in learning and memory after cocaine use were found[44]. However, other studies pointed out that cognitive deficits occur during consumption, but improvement appears during abstinence[45]. This contrasts studies concluding that deficits in memory function persist during abstinence[34].

Finally, some authors suggested that the alterations described in the functions of the hippocampus are not exclusively due to the use of cocaine[46] and that other factors and drugs should be analyzed.

Conclusions

The present work proves that there is a big amount of scientific evidence showing the importance of different neuroanatomical structures in cognitive and emotional processes of the human being and that the administration of cocaine can influence, modify and affect its development. First, articles related to the amygdala have been examined, demonstrating clear evidence of cocaine use in this brain structure, as well as its relationship with other brain structures. An example of this is the relationship with the hippocampus, which is necessary to establish emotional memories associated with drug use.

Regarding alterations in the PFC, several studies claim an increase in the activity of the PFC and, as a consequence, a development of impulsivity in the individual after the presence of stimuli related to the drug, which also affects decision-making.

Regarding the relationship between hippocampus, memory and cocaine consumption, the results also point to the fact that the consumption of the drug modifies the performance of memory-dependent tasks; nonetheless, studies to date are contradictory and show several positions. Perhaps the disparate methodology used in each of the analyzed experiments could be the cause of the discrepancy in the results obtained. On the other hand, memory is a very broad cognitive process, with many types and modalities. Thus, dealing with the relationship between the administration of cocaine, hippocampus and memory in a generic sense implicitly implies a great disparity, since studies point to different types of memory. As far as further research is concerned, a more specific empirical search on memory is proposed, for example, short-term, long-term, declarative, emotional, implicit, explicit memory... so that data will be more specific and appropriate for the aim of the study. In other words, more experiments in this area would be necessary to reach valid conclusions about the relationship between hippocampus, memory and cocaine consumption. Likewise, we encourage to delve into other types of drugs to see, for example, if Central Nervous System (CNS) depressant drugs like alcohol, or other psychostimulant drugs, such as ecstasy, have the same effects as cocaine on the mental and emotional processes here studied.

In any case, it seems evident that the administration of cocaine modifies the mental processes of the individual and that the study of these mental pro-

cesses and the anatomical structures involved can pose a great advance in the area of mental illness and cocaine addiction, thus providing knowledge for the progress of new possible therapeutic options.

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