UNIVERSIDAD SAN FRANCISCO DE QUITO USFQ

Colegio de Ciencias Sociales y Humanidades

Título del trabajo de integración curricular

The chronic use of marijuana and its effects on executive functions in emerging adulthood

.

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Psicología

Trabajo de integración curricular presentado como requisito
para la obtención del título de Licenciatura en Psicología

Quito, 4 de diciembre de 2019

UNIVERSIDAD SAN FRANCISCO DE QUITO USFQ

COLEGIO DE CIENCIAS SOCIALES Y HUMANIDADES

HOJA DE CALIFICACIÓN
DE TRABAJO DE INTEGRACION CURRICULAR

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Quito, 4 de diciembre de 2019

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Lugar y fecha: Quito, 4 de diciembre de 2019

RESUMEN

La legalización de la marihuana es una tendencia que ha ido en aumento en la última década en el occidente. La influencia de esta tendencia también ha llegado a Ecuador, donde las autoridades están trabajando actualmente en un proyecto de ley que legalizaría la cosecha, venta y consumo de marihuana medicinal. Por esta razón, es imperativo estudiar cómo el consumo crónico de marihuana afecta procesos neuropsicológicos, específicamente las funciones ejecutivas, de los adolescentes, ahora adultos emergentes. Algunos estudios recientes han encontrado una correlación existente del consumo de marihuana y deterioro en algunos procesos cerebrales. Aún así, no hay suficiente información específica sobre cómo se ven afectadas las funciones ejecutivas, razón por la cual el propósito principal de este estudio es evaluar las funciones ejecutivas en los usuarios crónicos de *Cannabis sativa.* Treinta participantes ecuatorianos que personalmente reportan tener problemas con un trastorno de consumo de marihuana serán reclutados para ser parte de la investigación, el cual se definirá como el uso de marihuana más días que no durante los últimos tres años. Basado en la revisión de literatura, se espera encontrar un deterioro global o específico por área en el funcionamiento ejecutivo de los participantes.

Palabras clave: drogas, marihuana, adultos emergentes, lóbulo frontal, funciones ejecutivas

ABSTRACT

The legalization of marijuana is a trend that has been increasing in the last decade around the West. The trend's influence has also reached Ecuador, where authorities are currently working on a law project that would legalize the harvesting, selling and consumption of medical marijuana. For this reason, it is imperative to study how the chronic smoking of marijuana is affecting the neuropsychological processes, specifically executive functions, of teenagers, now emerging adults. Some recent studies have found an existing correlation of consumption of marijuana and impairment on some brain processes. However, there is not enough information specifically targeting how executive functions are affected, which is why the main purpose of this study is to assess executive functions on chronic *Cannabis sativa* users. Thirty Ecuadorian participants who personally report having problems with marijuana use disorder will be recruited to be a part of the research, which will be defined as using marijuana more days than not for the past three years. Based on the literature review, it is expected to find global or area-specific impairment on the participants' executive functioning.

Key words: drugs, marijuana, emerging adults, frontal lobe, executive functions

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RESEARCH PROPOSAL

Problem Statement

For almost a century, substance abuse around the globe has become a major public health concern. Starting in the 1950s, the use of recreational drugs turned an already growing epidemic into a global health crisis. According to the National Survey on Drug Use and Health, around 20.5% of Americans aged 12 or older had been diagnosed with a substance use or abuse disorder in 2016 (Substance Abuse and Mental Health Services Administration, 2017). These numbers include the use of alcohol and other illicit drugs at the time, such as marijuana, cocaine, heroin, hallucinogens, inhalants, methamphetamine and others. The American Psychiatric Association (2013) defines Substance Use Disorder as "a cluster of cognitive, behavioral, and physiological symptoms indicating that the individual continues using the substance despite significant substance-related problems".

Although defining addiction in a specific and universal manner is challenging, Fields (2007) defines addiction based on two models: the choice and the disease model. The choice model states that the consumption of alcohol or other drugs is merely a choice by the user, which can probably be stopped whenever the user decides. On the other hand, the disease model states that addiction is, in fact, a chronic and progressive disease, presenting psychological and physical dependence. These definitions and models are currently used to diagnose and find the best intervention for a substance user.

Furthermore, research has shown that there are many possible causes for addiction. Regarding each model mentioned above, some causes of addiction can be stress-related experiences, like trauma; biological/genetic predisposition or even an insecure attachment to the person's primary caregiver. The attachment or parent-child bonding theory is widely used to treat addiction, since it explains how there is an impaired development of the child when

there is a poor bond with a parent. “The child may even suffer from depression as a result of times when he or she felt abandoned or rejected” (Fields, 2007).

Moreover, the legalization of marijuana is a trend that has been increasing in the last decade around the West. Currently, medical marijuana is legal in 28 states out of fifty states, as well as the District of Columbia and Puerto Rico (Rubin, 2017) in the United States. In a closer cultural context, recreational and medical marijuana has been legal in Uruguay since 2014, being the first country in the region that has allowed its citizens to harvest, sell and consume the drug (Traversa, 2019). The trend’s influence has also reached Ecuador, where authorities are currently working on a law project that would legalize the harvesting, selling and consumption of medical marijuana. Although at the moment the law has not passed yet, Ecuadorians will be ready in a near future to treat some chronic diseases like cancer, AIDS, fibromyalgia and arthritis with marijuana, increasing the use of the drug within the population.

In Ecuador, there is few information on substance use disorders. Most research and surveys are focused on the use or abuse of alcohol. However, the use of recreational and hard drugs is also affecting Ecuador's population, despite the lack of research on it. Specifically, the use of marijuana is currently limited to a certain personal-use amount, while the production and selling is not legal. The Ecuadorian government has created a possession table that specifies the amount of drug that a person can legally hold, which is 10 grams for marijuana, 2 grams for cocaine base, 1 gram for cocaine, 0.1 grams for heroin, 0.015 grams for ecstasy and 0.040 grams for amphetamines (Delgado & Muentes, 2018). Public opinion suggests that this table has enabled teenagers to use illicit drugs more often and with more freedom, increasing the substance use and abuse disorder rate in the country.

For this reason, it is imperative to study how the chronic smoking of marijuana is affecting the neuropsychological processes, specifically executive functions, of teenagers, now emerging adults. Hence, the current study aims to respond to the question, *"how and to what extent does marijuana affect the executive functions in the Ecuadorian emerging adults that meet the criteria for chronic use of marijuana?"*.

Objectives

This research aims to establish whether there is a relationship between chronic use of marijuana and executive functioning. The hypothesis of the current experiment states that marijuana use distorts executive functioning in participants, which means that it affects their behavioral inhibition, working memory and cognitive flexibility. Consequently, the main general objective of this research is to state how drugs are affecting people's body and minds, and marijuana is not an exception. Specific objectives include addressing of the problem exclusively in relation to executive functions, since there are some studies that conclude that marijuana affects cognitive processes in a broad way only. Also, this research will open possibilities to continue some studies on neurocognitive rehabilitation for these patients, jointly with psychotherapy.

Significance

There is limited research on the use and consequences of marijuana consumption in Ecuador. Drug use is common among teenagers around the world and research has shown that most drugs cause significant impairment in the human brain. However, most studies are outdated and have not found any relationship between the use of marijuana and cognitive processes. As time goes by, the legalization of marijuana is increasing worldwide, which also increases the interest of scientists to study its effects on brain processes. As a result, some recent studies have found an existing correlation of consumption of marijuana and

impairment on some brain processes. Still, there is not enough information exclusively on how executive functions are affected, and currently, society has little information on what the mental risks on the use of marijuana are, even less so in Ecuador.

Literature Review

Drugs and Alcohol

Sixty years ago, the true uprising of drugs started in the modern world. What historically was used to treat some medical diseases in a natural way by our ancestors, became the top hits for social movements of the era. Different types of drugs have their revolution in different decades throughout the last sixty years. Marijuana and hallucinogens, for instance, started to hit the streets and public meetings in the 1960s and 1970s, respectively, with the development of the hippie movement. These drugs were used by young people as a form of rebellion against the traditional values and civil violations. Whereas cocaine and synthetically produced drugs increased their popularity in the 1980s (Fields, 2007). In the beginning, cocaine was believed to cause psychological dependence only, but in the next years, its popularity brought addiction scientists big doubts on that belief, changing the concept and study of addiction in a whole way. By that time, laws were restricting the use and commercialization of these *new drugs*, which is why underground chemically modified drugs started to become popular, as way to trick the chemical composition of those banned drugs (Fields, 2007).

On the other hand, the history of alcohol in our society is way older compared to the history of other drugs. As yeast is the responsible for fermenting fruits in nature, it is believed that even our ancestor, the *Homo Sapiens* had contact with fermented fruits that were more appetizing and interesting than the rest of the fruits available in trees. Also, various chemical analyses have shown the presence of alcoholic recipes made approximately 9000 years ago,

based on fruits, rice and honey, almost like the wine we know today (Curry, 2017). Given alcohol's long story, its development into our modern society has been influenced by a lot of changes and adaptations, like different flavors, types, recipes, techniques and uses. Many years ago, alcohol was used by tribe leaders in order to obtain creativity and wisdom, as well as take advantages of its medical properties (Miller, 2014). Nowadays, alcohol is present in every aspect of popular culture, such as music, television, parties, movies, politics, social media and even religion, leading to "an unhealthy glorification of alcohol that encourages dangerous drinking habits" (Hoeg, 2019), along with other daily life use legal drugs that are also affecting the population.

Types of drugs

In order to understand the main differences between drugs, a brief classification of most used and well-known drugs is reviewed. Through the following classification, drugs are grouped based on the effects that they have in the Central Nervous System (CNS), in which we will find CNS depressants, CNS stimulants, hallucinogens, *Cannabis sativa*, and others.

CNS Depressants

The central nervous system depressants are known because of their high interaction with endorphins and GABA neurotransmitter in the brain. The effects of each drug may vary, but generally their main properties include: sedation, muscular relaxation, anxiolytics, anesthetic and anticonvulsive. These effects are caused mainly because of a decrease in blood pressure, heart rate, respiration rate and awareness. Larger doses alter perception and cause a decrease in brain functions and physical coordination, such as lethargy (Fields, 2007). An overdose of CNS depressants may even cause death, since the whole brain shuts down and is filled with inhibitory neurotransmitters, which eventually will reach vital areas such as the brain stem, where the cardiac and respiratory control areas rely. Alcohol, heroin, opiates and barbiturics can be considered within this category.

CNS Stimulants

The central nervous system stimulants have the opposite characteristics as the CNS depressants. These drugs mainly interact with serotonin, dopamine and norepinephrine inside the central nervous system, neurotransmitters responsible for brain cell connections, reward pathways and sympathetic nervous system activations. The main effects of these drugs include increased blood pressure, heart rate, respiration rate, awareness and alertness, talkativeness and excitement; as well as decrease in appetite, fatigue and boredom (Fields, 2007). An overdose of these drugs may excessively activate physical symptoms, especially those regarding the cardiovascular system, which can lead to arrythmias and heart attack. The drugs within this category are amphetamines, cocaine, crack, nicotine and caffeine.

Hallucinogens

These drugs are characterized for their psychedelic, psychotomimetic and psychotogenic properties. This means that they alter consciousness, mimic and produce psychosis (Fields, 2007). The main effects of these drugs include perception alteration, changing of feelings and emotions, flashes of light and hallucinations. However, there are several reports in which the effects of hallucinogens are very wide and can vastly vary depending on the context, the expectations and each personality. The main drugs that are included in this group are LSD and DMT available in some mushrooms, cactus and laboratory components.

Cannabis sativa

Although marijuana seems to fit best inside the category of hallucinogens related to its effects, there is a controversy in the last years about its categorization. A long time ago, it was believed that it belonged in this group, but the routes of administration, major effects, and possible damages differentiate it from the mentioned group. This is why, currently, all the types of marijuana, *Cannabis* derived, are inside an independent category. The

understanding of this categorization and the characteristics of marijuana is key to recognize the relationship it has with brain processes and executive functions, hence, the importance of this study.

There are more than 300 cannabinoids that have been synthetized from the *Cannabis* plant (Fields, 2007). The most active component found in the plant is called tetrahydrocannabinol (THC), which varies between the different types of plants that are consumed now. The more concentration of THC present in the plant, the more intense effects it produces. The effects that THC produces in the body include intensification of thoughts and feelings, relaxation, minor increase in heart rate, increased appetite, altered states of time and space and impaired short-term memory (Fields, 2007). Nevertheless, it is important to realize that these effects also vary a lot depending on the person, potency of the drug, the route of administration and expectation. This means that marijuana can induce depressant, stimulant and/or hallucinogen effects.

The variety of effects that marijuana has in the human body are primarily explained by the direct interaction of the cannabinoid with the endocannabinoid receptors (CB1 and CB2) in our human brain and other tissues. The endocannabinoid system, as it is named, is present in the CNS, peripheral nerves, blood cells, spleen, uterus and testicles (Du Plessis, Agarwal & Syriac, 2015). These receptors act with a G-protein, therefore, they can inhibit c-AMP or calcium channels. Also, the CB1 receptors are the ones that have been related to THC in the human body, since this type of receptors are mainly in the CNS. The union of THC in the CB1 receptor in the presynaptic neuron will cause a modulation of GABA neurotransmitter, which is an inhibitory substance for our brain cells (Harvey, 2012).

Marijuana is currently used for medical treatments in several countries worldwide. Its main medical properties are related to the treatment of severe nausea, weight loss, spasticity,

pain syndromes and glaucoma (Seamon, Fass, Maniscalco-Feichtl & Abu-Shraie, 2007). The increasing research programs on marijuana nowadays are giving promising results on the action that this substance can have when used under medical prescription and controlled doses. Other components, for example cannabidiol (CBD), are believed to lack the psychoactive effects of marijuana, which makes it a promising cannabinoid that will be used more in medical and psychiatric treatments like anxiety, chronic pain, mood symptoms and sleep complaints (Rong et al., 2017).

Conversely, the uncontrolled and chronic use of marijuana may lead to several adverse effects. Most of these effects are physical, while other cognitive effects are still controversy in research. The main effects of the use of chronic marijuana are related to a strong psychological dependence, withdrawal symptoms including irritability, restlessness, nausea, headaches, anxiety, and panic reactions (Fields, 2007). Concerning the physical adverse effects, there are reports of damage to the respiratory system like bronchial problems, sore throat and chronic coughing, immune system deficiency, cardiac effects including tachycardia, hypertension and syncope, and reproductive system effects such as decreased sperm motility and altered hormone levels in both genders. Also, most of marijuana smoke "contains 50-70% more carcinogenic ingredients than cigarette smoke that can lead to lung cancer" (Seamon et al., 2007).

Substance use and addiction

The term addiction or dependence has been part of the psychological treatment area for many years. However, the *DSM-5* has not included the term as a separate disorder in the new edition (contrary to the *DSM-IV)* since it can be prone to subjectivism between evaluators, therapists and other health professionals. Its main goal was to increase their validity and utility (Peer et al., 2012). Before, the manual contained different criteria between

substance dependence, substance abuse and substance intoxication. Still, in the new edition, substance dependence and substance abuse disorders were merged into one single diagnosis, substance use disorder (American Psychiatric Association, 2013).

Substance-related and addictive disorders inside the *DSM-5* include ten different types of drugs such as: alcohol, tobacco, caffeine, cannabis, opioids, hallucinogens, stimulants, sedatives, hypnotics and anxiolytics, inhalants, and others. The list of substance-related and addictive disorders includes those diagnosis that are identified by the consumption of the drug and those that are induced by the drug, such as withdrawal syndromes (American Psychiatric Association, 2013). Currently, the assessment and positive diagnosis for a substance use disorder takes into account a pathological pattern of behaviors that are related to the consumption of the substance. Also, the use of specifiers for the severity of substance use disorder is the one who will let professionals understand in which state of the substance use the patient is at the moment.

Still, there are some core characteristics of addiction that have been defined, which can increase interrater reliability within the addiction's treatment area. Fields (2007) describes three basic components of the addiction, analyzing from a behavioral perspective, defined as the three *C*s: compulsion, control and consequences. The first one, the obsessive-compulsive behavior with the substance, is described as a vicious cycle where users have an obsessive concern about the use of the substance, followed by an incessant use characterized as a compulsion. The second one is described as an inability to stop consuming the substance for at least 3 months and having failed attempts to cut it back. The third one is characterized as a continued use despite adverse consequences, which are usually influenced by some pervasive defense mechanisms of denial (Fields, 2007).

The same characteristics have been taken into account when creating the *DSM-5* criteria for substance use disorder. The criteria can be applied to the 10 different types of drugs mentioned, except for coffee. There are 11 criteria explaining the "problematic pattern of substance use leading to a clinically significant impairment or distress …" (American Psychiatric Association, 2013). The user needs to manifest this pattern by at least two of the criteria within a 12-month period. The first criterion refers to the user consuming larger amounts of the substance, or over a longer period than was intended. The second criterion refers to the presence of a persistent desire or unsuccessful efforts to cut down or control the use. The third criterion refers to the investment of a big amount of time in activities to obtain or use the substance or recover from its effects. The fourth criterion refers to the presence of craving or strong desire to use the drug. The fifth criterion depicts a recurrent consumption which affects responsibilities at home, school or workplace. The sixth criterion describes the behavior as a continued use despite having persistent problems because of the drug. The seventh criterion states giving up or reducing important activities in order to use the drug. The eight criterion refers to a recurrent use in situations where it is dangerous to do so. The ninth criterion states that the use is continued despite knowledge of having a problem with the substance. The tenth criterion defines the presence of tolerance, which is defined by the need of increased amounts to achieve intoxication or desired effect, or a diminished effect when using the same amount of the drug as before. Finally, the last criterion states the presence of withdrawal, which is defined by complying criteria for withdrawal syndrome, or using drugs in order to relieve or avoid its symptoms (American Psychiatric Association, 2013).

Etiology: risk and protective factors

Seeing addiction as a process, there are several determinants at the base that are usually related to biology, family system, and education. Numerous studies have shown that

gender is a risk factor for substance use. Males are more likely to consume alcohol and marijuana, especially during young adulthood (Stone, Becker, Huber & Catalano, 2012). This results also show that men are 1.4 times more likely to initiate the consumption and then advancing into heavier stages, like addiction. Race/ethnicity is another risk factor that shown to be associated with substance use disorder. A number of studies have also shown that Caucasians have an increased risk of experiencing a substance use disorder in young adulthood more than any other ethnic group. The group of Hispanics is the most relevant for the purpose of this study, being the least likely group to experience a substance use disorder when transitioning from abstaining in early adolescence to regular use during young adulthood (Gil, Wagner & Tubman, 2004).

Additionally, other factors influence on the reward circuit of neurotransmitters, precisely the dopaminergic circuits in the brain (Volkow et al., 2011). Mainly, the mesolimbic dopamine pathway is the responsible for the drug reward processes that are key to understanding the neuropsychological aspect of addiction. Several drugs, such as stimulants, nicotine, alcohol and marijuana have effects on these neurotransmitters, increasing the concentrations of dopamine in the circuits, thus, triggering a *high* or *euphoria* (Volkow et al., 2011). So, there are genetic factors that contribute to the transition from using a drug and being addicted, which are related to the dopaminergic pathways in the brain. Research has shown a genetic vulnerability for substance use disorders and dependence that is not only affecting the dopaminergic circuits, but also other neurotransmitters such as serotonin and GABA (Stone et al., 2012). This genetic influence is not caused by a single allele but by two different variations of alleles, which are transmitted throughout generations.

Considering the relationship of addiction and the family system, education and socioeconomic status (SES) are also factors to take into account when studying a subject.

"The most successful preventive approach is not to use drugs and alcohol, especially at early ages" (Fields, 2007). This means that parents have a crucial work in preventing children from becoming substance users or dependents in their future if they comply with several characteristics, such as not modeling substance use as a healthy approach, promoting positive activities, providing structure and discipline as well as encouraging consistent rules and family norms (Fields, 2007). Factors that encourage a healthy lifestyle and discourage drug use are considered as *protective factors*, the opposite to risk factors. High quality attachment or parent-child bonding is a protective factor, just like high education level, employment, emotional support, information sharing, internal locus of control, and positive perceptions of health status (Fields, 2007). Monitoring and good family relationships are key to protecting adolescents and young adults from using substances and becoming dependent after some time (Stone et al., 2012).

On the other hand, stressful situations are common inside unbalanced family systems. These life events include the death of a parent, ending a relationship, a parent away at war, illness or mental health issues, criminal justice problems or financial problems (Stone et al., 2012). The influence of the family system during adolescence is significant since this life stage is characterized by several changes, biologically, psychologically and socially. Although some young people are able to use substances without suffering any significant problems, any stressor can be a trigger to start substance use. "One-third of the 1520 24-year-old cohort participants had reported in adolescent interviews that they had used cannabis" (Swift, Coffey, Carlin, Degenhardt & Patton, 2008).

Substance use can be a gateway to family or social problems during adolescence, starting with an initial contact that is usually influenced by peers. The next phase is experimentation, where some effects of the drug are experienced, and if there is no protective

factor, the process will continue to a stage of excessive use and finally, the stage of addiction (Fields, 2007). It is important to assess adolescents and young adults' risk and protective factors for prevention and treatment, since early cannabis use is strongly linked to its abuse later in life. In an emerging adulthood study "more than half of the 521 adolescent users reported persistent use and two-thirds had commenced use by […] 15.9 years" (Swift et al., 2008).

Emerging adults

Adulthood is usually characterized by three main features: accepting responsibilities, making decisions independently, and getting financial independence (Papalia & Feldman, 2012). Yet, in the last years, technological development has forced adults to pursue a university or college degree in order to specialize their knowledge, which has affected their capacity of getting financial independence or full-time employment. This phenomenon, usually present in high income socioeconomic classes, has formed a new stage of human development, emerging adulthood. Emerging adulthood is a new concept that is of interest to many scientists since they have mixed features between adolescence and adulthood. This stage usually happens between the 18 and 25 years (Tanner & Arnett, 2009).

Since emerging adulthood is now considered a transitional stage between adolescence and adulthood, some features include risky activities during peak periods like "drinking, illicit drug use, drunk or drugged driving, and casual sexual behavior" (Schwartz & Petrova, 2019). The cognitive development during this stage is influenced by an exploratory manner of doing things, looking for possibilities and an opportunity to look for new and interesting activities. Individuals in emerging adulthood are experiencing the development of the brain's center for reasoning and decision making, which is usually reached by age 25. This means that emerging adults still remain sensitive to environmental conditions and experiences

(Tanner & Arnett, 2009). Plus, this also explains how emerging adults are very different from fully grown adults in relation to their information processing and emotion regulation. The physical status of emerging adults is commonly good; however, risky behaviors can have some negative consequences after this stage. In fact, most of the reported deaths within this age range are because of accidents (Papalia & Feldman, 2012).

Therefore, research on prevention science has shown that emerging adults are perfect candidates for *prevescalation*, which is "the goal of preventing escalation in problem behavior rather than seeking only to prevent initiation" (Schwartz & Petrova, 2019). This is because emerging adults usually already started consuming drugs during their late adolescence, which will have a huge impact on their adult lives if not treated or controlled. It is said that emerging adults still have a trend to increase their drug use behavior from a weekly basis to a daily basis (Schwartz & Petrova, 2019). Thereby, illicit drug consumption reaches its highest peak between 18 and 25 years. This rate tends to decrease once they reach full adulthood and the settling down process continues, *i.e.* getting married or having a stable employment. Moreover, marijuana is the most common illicit drug used by emerging adults (Papalia & Feldman, 2012). Emotional lability correlates with substance use disorders within this age range, increasing the rates of comorbid mood disorders, like depression and/or anxiety (Schwartz & Petrova, 2019).

Executive functions

Frontal lobes are responsible for the organization of cognitive processes, function that can be named *metacognition* (Ardila & Rosselli, 2019). The functions that frontal lobes carry include emotions, motor control, eye movement control, and attentional control together with executive functions. Usually, frontal lobes work in coordination with other areas in the brain, depending on the function; such as memory and visual interpretation on temporal and parietal

lobes or emotions on the limbic system. There are various executive functions that are related to intellect, thought and self-control (Anderson, Jacobs & Anderson, 2010). However, for the purpose of this study, two analyses will be done, one based on a simple categorization of the most predominant executive functions and another based on the anatomical-functional organization of these metacognitive processes.

Core Executive Functions

Usually, neuropsychological textbooks and articles include several different processes such as working memory, contextual memory, inhibition, planning, generativity and cognitive flexibility (Stefanatos & Fein, 2017). These six specific domains on executive functions can be recategorized as three core executive functions.

The first one is *inhibition*, which is related to the inhibition of automatic motor responses (Diamond, 2013). Inhibitory control as an executive function also includes the ability to select the attentional focus, control emotions and thoughts and be able to do what is appropriate within the social context. This means that the impairment on inhibitory control will affect the person by showing an impulsive behavior and low levels of attention on daily circumstances (Diamond, 2013). Generally, inhibition control is measured by giving activities with distractors and other temptations to stop doing them. The scores will be related to the capacity of the person to control impulses and continue with the activity, with minimum errors.

The second core executive function is working memory. This type of memory is not included inside long-term or short-term memory categories. On the contrary, it is another type of memory that usually holds information necessary for an immediate work or action. There are two types of working memory, verbal and nonverbal (Diamond, 2013). Also, working memory is the responsible for some top-down processes that include an input

perception, such as information received by the senses that can be related to learnt circumstances in order to make plans and decisions (Ardila & Rosselli, 2019).

The third core executive function is cognitive flexibility. This executive function is related to the other two core executive functions mentioned, since the main characteristic is the inhibition of a past perspective in order to accept and adapt to a new one, which will integrate information with working memory buffers (Diamond, 2013). Cognitive flexibility is also known as *shifting*, since in some activities, the person needs to shift their attention and concentration from one activity with certain rules, to a new one with different rules and characteristics (Ardila & Rosselli, 2019). This can be explained better by the assessment made by the Wisconsin Card Sorting Test.

Functional anatomy of Executive Functions

Some authors prefer to categorize executive functions by their anatomic localization, since it is believed that highly correlated executive functions are located in the same areas within the prefrontal cortex. This categorization is useful at the moment of assessing executive functions in patients, since damages to the prefrontal cortex can be focalized to a specific area. The global impairment of executive functions may not be a highly valid and reliable diagnosis, since the levels of disfunction can vary depending on which executive functions has been affected. Having said this, there are three main areas in the prefrontal cortex that are of interest for the purpose of this study.

Flores, Ostrosky & Lozano (2014) state that the dorsolateral prefrontal cortex is an important region responsible for planning, working memory, fluency, complex problem solutions and mental flexibility. This means that most of the core executive functions mentioned are highly correlated with this area. The prefrontal cortex is a specialized area of the frontal lobe that englobes different levels of association between inputs and other areas of the brain, such as posterior cortex and subcortical areas. Hence, the most complex and

superior cognitive processes are also related to the dorsolateral prefrontal cortex, such as metacognition and adaptation to change. Summing-up the main functions that scientists have found in this area are working memory and selective attention/response (Diamond, 2013). Hence, impairment in this area relates to dysexecutive syndrome.

The second region is the anterior prefrontal cortex, which is mainly responsible for inhibition processes, conflict solution and attentional regulation (Flores, Ostrosky & Lozano, 2014). This area is connected mainly to the anterior cingulate cortex, which is located in the limbic system. The relationship between the frontal cortex and the limbic system creates the bond for the regulation of emotions and thoughts, as well as impulsive behaviors that are dominated by the amygdala and the reptilian brain. Also, its connection to the limbic system is important for Theory of Mind (ToM) processes, which are not part of executive functions, but still very important during neuropsychological assessment, especially for autism spectrum disorders (Stefanatos & Fein, 2017). In summary, the anterior prefrontal cortex is highly related to planning and self-initiated behavior. Consequently, impairment in this area leads to apathy and abulia.

Finally, the third area is the orbitofrontal cortex. This area is located right in front of the olfactory cortex and is also highly related to the limbic system (Flores, Ostrosky & Lozano, 2014). Because of this, the orbitofrontal cortex is responsible of processing and regulating emotions, which includes behavioral regulation. Also, circuits regarding risk-benefit decision making processes are within this cortex, since this area can also detect positive or negative changes in environmental conditions (Diamond, 2013). So, the orbitofrontal cortex is mainly responsible for decision-making processes. Thus, impairment in this area leads to disinhibition syndrome.

Methodology and Research Design

Design

The current study aims to determine how and to what extent marijuana affects executive functions in Ecuadorian emerging adults that meet the criteria for chronic use of marijuana. The results found on this research will be analyzed quantitatively through a neuropsychological battery that consists of 15 different psychometric evaluations for different executive functions. There will be two different groups, a control group and a group of chronic marijuana users evaluated under the *DSM-5* diagnostic criteria for substance use disorder, a demographic questionnaire, the *CAST* and the *BANFE-2*.

The comparison and analysis of results will be done between subjects in two different levels. The first level of comparison will be made using average grades in each of the three specific areas that the battery assesses: orbitofrontal and medial prefrontal cortex, dorsolateral prefrontal cortex and anterior prefrontal cortex (Flores, Ostrosky & Lozano, 2014). The second level of comparison will be done with the average total results of the executive functions area that the battery assesses, which is considered a global scoring of the whole battery. Scores obtained for each area and for the global area of the battery will be compared between the control group and the experimental group in order to obtain the significant differences for the numeric data that will test the hypothesis.

Population

30 Ecuadorian participants who personally report having problems with marijuana use disorder will be recruited to be a part of the research, which will be defined as using marijuana more days than not for the past three years. Both genders will be allowed to be participants, with a preferred ratio of 15 males to 15 females. The age range of participants

will be between 18 and 25, with an average of 21.5 years old. Participation is voluntary and each one will be tested individually.

Inclusion criteria:

- Functioning role in society, i.e. gainful employment or regular attendance to college, university or technical education.

Exclusion criteria:

- Use of any other hard drug (cocaine, crack, meth, heroin) in the past year.
- Present any co-occurring mental disorder in the past four years.

Research Tools

Informed consent will be signed at first instance by all participants who want to join. Then, participants will be diagnosed under the *DSM-5* diagnostic criteria for substance use disorder (addiction). Later, a demographic questionnaire will be given to each participant in order to assess the rest of inclusion/exclusion criteria. Next, the *CAST* will be applied to each of the participants already inside the experiment in order to obtain qualitative characteristics of the chosen sample for discussion and analysis purposes. Finally, the neuropsychological battery *BANFE-2* will be applied individually to every participant.

DSM-5

The Diagnostic and Statistical Manual of Mental Disorders (DSM-5) is a diagnostic tool with the main objective of assisting trained clinicians in the analysis of a wide classification of mental disorders in order to obtain the most suitable diagnosis for each patient, thus the most adequate treatment option for them (American Psychiatric Association, 2013). Most of the criteria found in the manual constitute a practical guide to comprehend the definition of a mental disorder as well as other “cognitive, emotional, behavioral, and physiological” (American Psychiatric Association, 2013) traits that are related to each

diagnosis. These traits can also be analyzed as some signs or symptoms that are present in an underlying mental disorder. Other additional information for each disorder includes developmental history, risk factors within genetics or society and correlation with other neuropsychological and physiological processes. For the purposes of this research, the criteria used to assess participants will be those included under the category of *cannabis-related disorders*, specifically the *cannabis use disorder* (American Psychiatric Association, 2013).

Demographic Questionnaire

For the purpose of this research, a demographic questionnaire will be developed in order to assess additional inclusion/exclusion criteria within the participants. The demographic questionnaire will be included along with the *CAST*, where personal information will be asked to each of the participants. The information which the demographic questionnaire intends to collect will be age, sex, country of birth, years of education, current occupation, employment/studying status, and two yes/no questions on previous mental health diagnoses and consumption of any other hard drug in the last year.

CAST

The Cannabis Abuse Screening Test (CAST) is a self-administered questionnaire that assesses problematic use of cannabis (Cuenca-Royo et al., 2013). Its main purpose is to describe different aspects of harmful cannabis use, as well as screening of what could be stated as a problematic cannabis use. It was developed by the French Monitoring Centre for Drugs and Drug Addictions, with a sensitivity of 0.93 and a specificity of 0.81 (Annaheim & Legleye, 2017). There is a Spanish version that is widely used mainly in Spain, which is short and easy to respond, with a lot of components that are usually important within the young and young-adults population.

The *CAST-f*, used in the present research, is composed by 6 items and assesses the frequency of cannabis-related events within the last 12 months which are: recreational use,

memory problems, attempts and motivations to reduce or stop the use of cannabis, and other problems related to the use of cannabis. Each item is answered on a Likert scale from 0 to 4, where 0 means *never* and 4 means *always* (Cuenca-Royo et al., 2013). The total score over 24 is taken into account for the whole test, and cutoffs are 7 for moderate use and 9 for dependence (Cuenca-Royo et al., 2013).

BANFE-2

The Neuropsychological Battery of Executive Functions and Frontal Lobes-2 (Batería Neuropsicológica de Funciones Ejecutivas y Lóbulos Frontales-2, BANFE-2) is a psychometric battery used to assess different neuropsychological functions of cognitive processes that are under the control of the frontal lobes. Hence, executive functions are also included among these processes. *BANFE-2* presents a large number of neuropsychological tests with high reliability and validity to assess frontal lobe processes (Flores, Ostrosky & Lozano, 2014) which are important for daily life activities such as planification, regulation and control of other psychological processes, as well as coordination and selection of strategies and behaviors. It was developed in Mexico by researchers at Universidad Nacional Autónoma de México and is also officially validated in Colombia.

This tool aims to evaluate 15 processes related to executive functions in Spanish speakers, from 6-year-old children up to adulthood. All these 15 processes are divided in three specific areas, according to their functional and anatomical relationship. The first area is the orbitofrontal and medial prefrontal cortex, where three activities are measured such as Stroop test, gambling card game, and mazes. The second area is the dorsolateral prefrontal cortex, where nine activities are measured such as self-directed signaling, visuospatial working memory, alphabetical word ordering, card sorting, mazes, Hanoi tower, consecutive addition and subtraction, and verbal fluency. The third area is the anterior prefrontal cortex,

where three activities are measured such as semantic sorting, selection of proverbs, and metamemory (Flores, Ostrosky & Lozano, 2014).

Each functional-anatomical area specified has its own scoring. The first step is to get the raw scores for each activity, and then normalize those scores with the tables provided in the Manual (Flores, Ostrosky & Lozano, 2014). Calculation of scoring can be done manually or electronically through the *BANFE-2* website, where in the end, total scores for each area will be interpreted within the categories high normal, normal, mild-moderate alteration, and severe alteration. There are also total raw and normalized scores for the whole battery, which give a global diagnosis of executive functioning in the participant. It is important to state that normalized scores depend on age and the number of years of formal education that the participant has.

Data collection

Recruitment of participants will be done through social media, advertisements in different universities and direct visits to rehabilitation centers or mental health clinics. Participants who are currently battling an addiction, either on treatment or not, will receive the invitation to participate in the experiment from a USFQ psychology student. There will be a $20 financial incentive draw comprising all participants who are included in the investigation.

The first step when receiving an interested participant is signing the informed consent where all the information, purposes and risks of the investigation will be explained. If the participant wants to continue, an interview will be done, where *DSM-5* criteria will be evaluated in order to give a proper diagnosis of *cannabis use disorder*. This step would have an approximate duration of 10 minutes. If approved, the next stage is the application of screening tests in order to obtain more personal and substance-use related information. That

is the application of the demographic questionnaire so as to get personal information regarding the inclusion/exclusion criteria. Completing the questionnaire will take approximately 5 minutes. Once the investigator confirms the participant is in compliance with all the inclusion criteria, and does not comply with the exclusion criteria, the next screening test will be applied. Since the *CAST* is a short self-administered test, it will be given to the participant after explaining what it consists of and how to respond to the items. This screening test will take approximately 5 minutes. Finally, the *BANFE-2* will be administered by the investigator, starting in the order offered by the Manual (Flores, Ostrosky & Lozano, 2014) and answer sheets, which is:

1. Mazes
2. Self-directed signaling
3. Alphabetical word ordering
4. Consecutive subtraction
5. Consecutive addition
6. Card sorting
7. Semantic sorting
8. Stroop form A
9. Verbal fluency
10. Gambling card game
11. Selection of proverbs
12. Hanoi tower
13. Metamemory
14. Visuospatial working memory
15. Stroop form B

Some activities have time limits, while others do not. The approximate time that will take to complete the whole battery is 50 minutes, although it can extend some more when working with severe impaired patients (Flores, Ostrosky & Lozano, 2014). The investigator needs to follow the protocol in the Manual at all times so information is read accurately, and time limits are being respected. At the end, participants will be thanked for their time to the current research, and then scoring will be calculated to test the hypothesis. The total time it will take for a participant to complete all the stages is approximately 1 hour (60 minutes), in only one session.

Data analysis

Data analysis will be done in different aspects. The first aspect will be comparing average scores and standard deviations from the normalized subtotal scores for each area, between the control group and the experimental group. These are orbitofrontal and medial prefrontal cortex averages, anterior prefrontal cortex averages, and dorsolateral prefrontal cortex averages. Then, an analysis and comparison will be made between the total normalized score average for executive functions battery between both groups. Comparing the average scores in each area will determine if there is a specific effect of the chronic use of marijuana within the different executive functions. In contrast, comparing the total average scores between both groups will determine if there is a global impairment of these functions. However, it is also necessary to further analyze the averages for each area subtotal and the global average between the two groups in order to identify if there are *significant* differences in the scores obtained. So, four independent groups t-tests will be made and analyzed for each score. These analyses will test the following null hypothesis: there are no differences on executive functioning between chronic users of marijuana and control groups. Deeper discussion and data analysis will include p-values and effect sizes (Cohen's d).

Ethical Considerations

The Institutional Review Board for Human Research at Universidad San Francisco de Quito (Comité de Ética USFQ) will examine the present study and verify that all ethical considerations are being respected at all times. An informed written consent will be prepared for the submission of this research proposal, which has to be approved by the board. All participants will be given the approved informed written consent which will explain all the objectives, risks and methods of the current study. Each participant who is personally encouraged to join the investigation will receive an identification code in order to maintain the participant's identity and personal information fully confidential and anonymous. All the information collected in this study will be used for research purposes only. Participation is strictly voluntary with no negative implications for those who choose not to participate or retire at any time during the investigation. This means that, if for any reason any participant feels the need to leave the study, he or she is free to do so.

Discussion

The current research aims to answer the question *"how and to what extent does marijuana affect the executive functions in the Ecuadorian emerging adults that meet the criteria for chronic use of marijuana?".* Numerous research have shown that the chronic use of alcohol and other hard drugs affect brain processes in different ways, mainly cognitive functions such as attention and memory. However, it is imperative to expand research on how a commonly used drug, such as marijuana, is affecting brain processes. Marijuana consumption has been increasing in the last years since therapeutic and recreational uses are been legalized around the globe (Du Plessis et al., 2015). Therefore, it is relevant for public health authorities to have information on the possible side effects on brain processes, specifically on executive functions, so that consumers can be better informed before deciding

to start or continue using *Cannabis* for different purposes. The emerging adulthood target group is also pertinent for the current research, since marijuana is the most consumed drug during adolescence (Papalia & Feldman, 2012), which means that emerging adults (18 to 25 years old) will be directly related to the consumption of the drug in previous years.

Endocannabinoid receptors play an important role in a lot of processes regarding the CNS (Harvey, 2012). The mimetic action of *Cannabis* with these receptors is the main reason why its effects on brain processes are of interest for research. Although intelligence quotient (IQ) has been studied in chronic use of some drugs (including marijuana), executive functions are other frontal lobe processes that are highly affected by the mentioned drug. Executive functions are important for human performance, since it includes all decision-making processes that are made on a daily basis (Anderson et al., 2010). Also, it is known that dopaminergic pathways inside the brain are responsible for the addiction process as well as euphoric symptoms. In fact, frontal lobes are also included inside dopaminergic pathways in the brain (Volkow et al., 2011), which increases the possibility of an impairment on frontal lobe functioning when using a drug chronically. Therefore, there is evidence of a link between addiction or substance abuse and frontal lobe processes in the brain, *i.e.* executive functions.

Based on the literature review done for this research, the application of a battery of neuropsychological tests that evaluate executive functions is essential to assess what is the real effect of the chronic use of marijuana on the aforementioned functions. There is even a stronger bond between executive functions and the use of drugs, which will open the doors for future investigation regarding causality, to determine if impairment on inhibition is the reason why certain people abuse the drug, or if the chronic abuse of the drug causes impairment on inhibition and other executive functions. Also, if decision-making processes

are affected, there could be a reason to choose consuming a drug over avoiding it. As expected, an impairment on global executive functioning will be found in patients. This global impairment will include low scores for functioning on working memory and selective attention in the dorsolateral prefrontal cortex, inhibition and planning on the anterior prefrontal cortex, and decision-making on the orbitofrontal cortex (Flores, Ostrosky & Lozano, 2014). Nevertheless, area-specific impairment can also be found in some users, since there is no concrete link between the areas mentioned in a neuropsychological functioning matter.

Public health priorities are usually preventing diseases. But once the disease is present in the population, the main priority switches to healing or reducing pain. Regarding drug use and abuse, specifically marijuana, the main priority should include reducing dysfunctional behaviors that will perpetuate symptoms chronically or even increase the risk of premature death. Promptly finding the impairments on human functioning caused by a chronic use of marijuana will help authorities build new policies that include psychotherapy and possible neurocognitive rehabilitation therapy, which will reduce the impact of the drug on users. Nowadays, Ecuador has poor policies on addiction treatment (Delgado & Muentes, 2018), which is why is important to contribute with more research data on different drugs and intervention mechanisms, so that future policy-makers can take into account the cognitive problems that society is exposed to because of the legalization of medical and/or recreational use of marijuana.

Strengths and limitations of proposal

There is an important strength that should be identified in the current study. *BANFE-2* permits evaluators make a differential diagnosis between the distinctive functions that are carried by the frontal lobes. Different executive functions are being evaluated in this research,

and sometimes, it is difficult to understand the dissimilarity between these functions with separate tests that do not give the chance to integrate results. Also, the information collected for each function is related to their anatomical area within the prefrontal cortex, which will help on treatment focus for this group of patients.

Nevertheless, there are some limitations that affect the precision of the results. The first limitation in this study regards the rapport between the participant and the evaluator. Although the first activities are simple, self-administered and do not require special training for evaluators, the context of relationship between the participant and the evaluator may alter the participant's performance, hence, the results. For the main activity that is intended to assess all the functions of interest, *BANFE-2*, there is a standardized protocol that minimizes the evaluators influence on the participant. However, a special training is required for this.

Finally, the second limitation of this study is related to the population. Most participants were from Quito, the city where the study was advertised and performed, which fails to accurately represent the Ecuadorian population. Also, the sample size was not large enough, which means that results may not be reliable for the whole population that this research intends to study. Lastly, *BANFE-2* is a valid battery in Mexico and Colombia, but there is no strong validation of this test for the Ecuadorian population, which means that it may slightly change some real scores of the population, regarding the normalized values.

Future implications

Future research should be aimed to represent the whole Ecuadorian population, either focusing on different regions of the country or making larger and more diverse samples. Additionally, further analysis of the impaired functions should be made. Usually, participants within the selected group are seeking for therapy and abstinence periods. Retesting the participants after these periods (approximately one year later) will be essential to understand

if the effects found are reversible or not. Finally, the author hopes that this research opens the doors for more neurocognitive implications on substance use and abuse populations, specifically on neurocognitive rehabilitation tools and treatments plans for the areas that have been affected; so in the future there can be a combination between psychotherapy (e.g. cognitive-behavioral/psychodynamic therapy) and neurocognitive rehabilitation in addiction clinics.

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ANNEX A: Informed consent form and application to the IRB at USFQ

UNIVERSIDAD SAN FRANCISCO DE QUITO USFQ

Formulario de Consentimiento Informado por escrito

Título de la investigación: The chronic use of marijuana and its effects on executive functions in emerging adulthood.
Organizaciones que intervienen en el estudio: Universidad San Francisco de Quito
Investigador Principal: Amilcar Mateo Cahueñas Bernal, 0992663080, acahuenasb@estud.usfq.edu.ec
Co-investigadores: n/a

DESCRIPCIÓN DEL ESTUDIO
Introducción *Debe tomarse en cuenta que el lenguaje que se utilice en este documento no puede ser subjetivo; debe ser lo más claro, conciso y sencillo posible; deben evitarse términos técnicos y en lo posible se los debe reemplazar con una explicación*
Este formulario incluye un resumen del propósito de este estudio. Usted puede hacer todas las preguntas que quiera para entender claramente su participación y despejar sus dudas. Para participar puede tomarse el tiempo que necesite para consultar con su familia y/o amigos si desea participar o no. Usted ha sido invitado a participar en una investigación sobre los efectos en las funciones ejecutivas del consumo crónico de marihuana.
Propósito del estudio Incluir una breve descripción del estudio, incluyendo el número de participantes, evitando términos técnicos e incluyendo solo información que el participante necesita conocer para decidirse a participar o no en el estudio
Se reclutarán 30 participantes con el objetivo de determinar cómo y en qué medida el consumo crónico de marihuana afecta las funciones ejecutivas de los adultos jóvenes.
Descripción de los procedimientos para llevar a cabo el estudio Breve descripción de cada actividad en la que participarán los sujetos y el tiempo que tomará. No describir procesos en los que los participantes no tomarán parte.
1. Reclutamiento de participantes voluntarios que cumplan con los criterios requeridos para el estudio. 2. Realizar una entrevista de diagnóstico para evaluar los criterios de inclusión y determinar el consumo problemático de marihuana, durante 10 minutos. 3. Aplicación de 2 evaluaciones globales: datos demográficos y CAST (consumo de marihuana), durante 10 minutos. 4. Aplicación del BANFE-2, una prueba de medida de funciones mentales, durante 50 minutos. 5. Análisis de datos y conclusiones.

Riesgos y beneficios Explicar los riesgos para los participantes en detalle, aunque sean mínimos, incluyendo riesgos físicos, emocionales y/o sicológicos a corto y/o largo plazo, detallando cómo el investigador minimizará estos riesgos; incluir además los beneficios tanto para los participantes como para la sociedad, siendo explícito en cuanto a cómo y cuándo recibirán estos beneficios
No existen riesgos significativos para la salud mental o física de la persona. En algunas ocasiones, por el tiempo de aplicación de la batería neuropsicológica de funciones ejecutivas, podría presentarse cansancio, fatiga, dolor ocular o dolor de cabeza. Sin embargo, estos síntomas se podrán minimizar al tomarse un descanso de aproximadamente 10 minutos para poder continuar con el resto de las pruebas. Los participantes se beneficiarán de este estudio ya que no existen datos sobre el consumo de marihuana y sus efectos negativos en las funciones ejecutivas de los adultos emergentes. Por lo tanto, en Ecuador, hacen falta campañas de información y educación para que las personas sepan las consecuencias reales del consumo de la sustancia. Asimismo, los resultados y las conclusiones sacadas de este estudio permitirán

crear un nuevo programa de intervención y tratamiento que incluya psicoterapia y rehabilitación neurocognitiva para las funciones afectadas.

Confidencialidad de los datos *Debe describirse cómo se protegerá el anonimato de los participantes, y también cómo se garantizará la seguridad de los datos en todas las etapas del estudio: reclutamiento, ejecución, análisis, publicación, postestudio (almacenamiento). Es importante explicar quién será el custodio de los datos recolectados..*

Para nosotros es muy importante mantener su privacidad, por lo cual aplicaremos las medidas necesarias para que nadie conozca su identidad ni tenga acceso a sus datos personales:
1) La información que nos proporcione se identificará con un código junto con su nombre y se guardará en un lugar seguro donde solo los investigadores mencionados al inicio de este documento tendrán acceso. Una vez finalizado el estudio se borrará su nombre y se mantendrán solo los códigos.
2) Se removerá cualquier identificador personal que permita su identificación al reportar los datos obtenidos.
4) Su nombre no será mencionado en los reportes o publicaciones.
5) El Comité de ética de la investigación en seres humanos (CEISH) de la USFQ, podrá tener acceso a sus datos en caso de que surgieran problemas en cuando a la seguridad y confidencialidad de la información o de la ética en el estudio.
6) Al finalizar el estudio los datos serán almacenados en una carpeta confidencial en la nube electrónica del investigador por 15 años.

Derechos y opciones del participante

Usted puede decidir no participar y si decide no participar solo debe decírselo al investigador principal o a la persona que le explica este documento. Además aunque decida participar puede retirarse del estudio cuando lo desee, sin que ello afecte los beneficios de los que goza en este momento.
Usted no recibirá ningún pago ni tendrá que pagar absolutamente nada por participar en este estudio. Sin embargo, como forma de agradecimiento por su tiempo y esfuerzo, se incluirá su contacto en un sorteo de $20 que incluye a todos los participantes del grupo.

Procedimientos para verificar la comprensión de la información incluida en este documento

- ¿Puede explicarme cómo va a participar en este estudio?
- ¿Qué hace si está participando y decide ya no participar?
- ¿Cuáles son los posibles riesgos para usted si decide participar? ¿Está de acuerdo con estos riesgos?
- ¿Qué recibirá por participar en este estudio?
- ¿Hay alguna palabra que no haya entendido y desearía que se le explique?

Información de contacto

Si usted tiene alguna pregunta sobre el estudio por favor envíe un correo electrónico a acahuenasb@estud.usfq.edu.ec, que pertenece a Mateo Cahueñas Bernal.

Si usted tiene preguntas sobre este formulario puede contactar al Dr. Iván Sisa, Presidente del CEISH-USFQ USFQ, al siguiente correo electrónico: comitebioetica@usfq.edu.ec

Consentimiento informado	
Comprendo mi participación en este estudio. Me han explicado los riesgos y beneficios de participar en un lenguaje claro y sencillo. Todas mis preguntas fueron contestadas. Me permitieron contar con tiempo suficiente para tomar la decisión de participar y me entregaron una copia de este formulario de consentimiento informado. Acepto voluntariamente participar en esta investigación. Al firmar este formulario, usted acepta voluntariamente participar en esta investigación. Usted recibe una copia de este formulario.	
Nombres y apellidos del participante: Firma /huella del participante	Fecha CC
Nombres y apellidos del testigo: Firma /huella del testigo	Fecha CC
Nombres y apellidos del investigador: Mateo Cahueñas Bernal Firma del investigador	Fecha: CC: 1720870946
Negativa del consentimiento	
Nombres y apellidos del participante: Firma /huella del participante	Fecha CC
Nombres y apellidos del testigo: Firma /huella del testigo	Fecha CC
Nombres y apellidos del investigador: Firma del investigador	Fecha CC
Revocatoria del consentimiento	
Nombres y apellidos del participante: Firma /huella del participante	Fecha CC
Nombres y apellidos del participante: Firma /huella del testigo	Fecha CC
Nombres y apellidos del investigador: Mateo Cahueñas Bernal Firma del investigador	Fecha CC: 1720870946

ANNEX B: Demographic Questionnaire and Cannabis Abuse Screening Test (CAST)

Código: _____

CAST (Cannabis Abuse Screening Test) en Español

¿Con qué frecuencia te ha ocurrido algo de lo que se describe a continuación en los últimos 12 meses?

	NUNCA	RARA MENTE	DE VEZ EN CUANDO	BASTANTE A MENUDO	MUY A MENUDO
1. ¿Has consumido *Cannabis* antes del mediodía?	☐	☐	☐	☐	☐
2. ¿Has consumido *Cannabis* estando solo/a?	☐	☐	☐	☐	☐
3. ¿Has tenido problemas de memoria al fumar *Cannabis*?	☐	☐	☐	☐	☐
4. ¿Te han dicho tus amigos/as o miembros de tu familia que deberías reducir el consumo de C*annabis*?	☐	☐	☐	☐	☐
5. ¿Has intentado reducir o dejar de consumir *Cannabis* sin conseguirlo?	☐	☐	☐	☐	☐
6. ¿Has tenido problemas debido a tu consumo de *Cannabis* (disputa, pelea, accidente, mal resultado escolar, etc.)? ¿Cuales?:	☐	☐	☐	☐	☐

Código: _____

Cuestionario de Datos Demográficos

Edad (años y meses): ____ años y _____ meses.

Sexo: Masculino ____ Femenino ____

País de Nacimiento: _____

Años de educación (marque con una X en el cuadro correspondiente):

Universitaria o Superior completa (>17 años)	
Bachillerato completo (>12 años)	
Primaria completa (>8 años)	
Primaria incompleta (especifique el número de años): _____	

Ocupación actual: _____

Marque con una X si actualmente estudia o trabaja, o ambas.

Estudio: _____ Trabajo: _____

He tenido un diagnóstico previo realizado por un profesional en salud mental (psicólogo, psiquiatra, neurólogo, etc.): Sí ___ No ___

He consumido cualquier droga fuerte (cocaína, heroína, éxtasis, metanfetaminas) en los últimos 12 meses: Sí ___ No ___