Cannabis and Psychiatric Pathology: An Update

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ABSTRACT

In the last 2 to 3 years a significant number of articles about psychological consequences of cannabis use in humans have been published. These articles address topics such diverse topics as chronic use of cannabis and its relationship to schizophrenia, cognitive deterioration, anxiety, and the existence of cannabis dependence. The results show that cannabis use significantly increases the risk of developing any of the abovementioned disorders. Although, these results require further analysis in order to confirm or reject them.

All this is happening at a time in which there are an increasing number of cannabis consumers and the medical community is trying to establish the possibilities of cannabis as therapeutic agent. We should not forget the undesirable effects when we take up a position in the debate on legalization of cannabis.

INTRODUCTION

The psychological effects of cannabinoids have been known for a long time; although, the first scientific description of such effects is to be found at the end of the nineteenth century. It was carried out in 1845 by Moreau, who described cannabis effects after having consumed the substance himself.

Since then the subject has been largely studied, at times referring to the mental after-effects of marijuana use and at other times discussion or research on this issue seemed to be finished. Over the past few years, we are witnessing a new period of intense work in this field largely due to the discovery and analysis of the endocannabinoid system and the possible therapeutic application of cannabinoids. Research continues to offer much to discover and discuss.

FACTORS INFLUENCING THE PSYCHOLOGICAL EFFECTS OF CANNABINOIDS

Routes of Administration

The psychological and behavioral effects of marijuana vary according to the route of administration (smoke, intravenous, or oral). When smoked, it is absorbed in a few seconds and very quickly reaches the brain, in a form that is highly soluble in lipids. This quick absorption causes most of the negative acute effects that appear after consuming the drug in this way. The peak in blood appears once the cigarette has been completely smoked.[1-3]

The oral use of THC or marijuana causes the appearance of the maximum peak in blood to be delayed between 1 to 3 hours after an oral dose.[1,4] Consequently, the beginning of the psychological effects is far quicker when it is consumed as a cigarette. The average effect of THC is estimated to be of approximately 20 hours.

Dose

The dose-dependant effect pattern of cannabinoids is well known. In low doses cannabis acts as a sedative; in high doses, it is a hallucinogen. Consumers frequently have access to doses where the concentration is unknown. Therefore, the results produced after using cannabis can be different from those expected, for example, the appearance of psychotic symptoms.[5]

Tolerance

Another feature that can modify the effect of marijuana is the tolerance phenomenon. Tolerance to its different effects (cardiovascular, autonomic, etc.) is rapidly acquired after repeated use of marijuana, both smoked and orally consumed. The tolerance disappears quickly, too, if cannabis use is eliminated.[6]

The effect of inverse tolerance has also been described. This means that the impact is stronger with smaller doses, which inevitably leads to the appearance of undesirable effects, especially those related to psychological and behavioral aspects.

Experience and Use Expectations

It is not uncommon to see young people, in emergency rooms, who, after their first contact with cannabis, show anxious reactions, occasionally motivated by the sight of similar symptoms in friends.

The cannabis user tends to expect the outcome to be similar to those that he has either heard about or felt before during past use.

An experienced marijuana user can even control and adjust the dose necessary to obtain the effects he wishes, as well as avoid the unwanted ones.[7,8]

Personality Features

Many of the cannabis users seek to overcome various difficulties posed in their own lives through the use of the substance[9] A number of research works have correlated the use of cannabis with the appearance of schizotypal personality disorders,[10-12] which greatly increase the hazard of evidencing psychotic symptoms in high-risk individuals.

Some authors[13] have found a greater use of cannabis, in individuals who show impulsive and anti-social traits.

Interaction with Other Substances

Marijuana shares several metabolic traits with other substances of common substances, such as alcohol, tobacco, and other therapeutic drugs, which makes interactions inevitable. For example, THC and cannabidiol inhibit the metabolism of substances metabolized by the hepatic system of oxidase enzymes.[14-16] The absorption and clearance of other substances taken at the same time as marijuana are affected (slowed down) depending on the time and sequence of use, and even according to previous intake. For example, the use of alcohol just after marijuana use causes a peak in blood that is far lower than the peak that results when it is consumed one hour before marijuana use. This is due to the fact that THC slows down gastric emptying, as it does with alcohol absorption.

REASONS FOR CANNABIS USE

Through its consumption the cannabis user seeks certain effects widely attributed to this substance, such as euphoria, increase in sociability, decrease in anxiety caused by certain social situations (shyness, embarrassment), spontaneity, or the mere social identification with a specific group.[9] This pattern of behavior (the intake as a means of achieving certain specific ends) appears to be typical among users of any illicit drug. In the case of cocaine or synthetic drugs, the expected effect is the generalized stimulation of physical and psychological functions, while heroine is expected to

induce relaxation.

The previous discussion refers to a healthy population. As far as schizophrenics are concerned, it seems to be clear that the reasons for cannabis use are explained by the so called self-medication hypothesis.[17] Such hypothesis assumes that in the presence of a specific mental disorder, the patient turns to a substance that will free him from the suffering caused by his condition. When taking cannabis, these consumers seek to ease psychological tension, aimed at the disappearance of disturbing auditory hallucinations, and want to overcome apathy and aboulia, to improve social relations (the schizophrenic subject tends to social isolation) as well as to overcome the depressive phase accompanying this disorder.[18,19] Initially they seem to succeed; however, they soon develop tolerance to the above mentioned effects, and this leads these patients to a situation in which they have to increase their dose and frequency in consumption. The result of all this is an aggravation of their disease, with serious consequences for the subject.[20]

MENTAL AND BEHAVIOURAL EFFECTS

Common Acute Effects

Mental and behavioral effects of marijuana include a state of well being (euphoria), a feeling of relaxation, perception alterations (changes in shape, color and brightness, time seems slower), loquacity, and an increase in sociability within a specific social environment.[21]

On the other hand, other habitual results from cannabis use include: the deterioration of recent memory, motor coordination (ie, impaired driving) and other psychomotor abilities; difficulty concentrating, a state of stupor (being "stoned"); degradation of reactive capacities; decrease in mental activity; and an alteration of peripheral vision.[4,22-24]

Very soon after repeated exposure to marijuana tolerance to a number of subjective and psychological results appears.[22,25] Thus, their intensity is established, not only by the THC dose, but also by past experiences, the user's expectations, the atmosphere, and the differing sensitivity typical of each individual.[26] After an average, dose, mental effects are easily quantified and measured for a few hours (normally no longer than 4 to 6 hours).[16,23] Some studies describe cognitive effects as remaining after 24 hours, even after a single smoked or oral dose.[22,24] Venous levels of THC and other cannabinoids correlate poorly with the intensity and type of intoxication.[1,2,27]

ADVERSE MENTAL EFFECTS

Acute Adverse Mental Effects with Less than 5 Years of Use

The occasional use in sensitive, inexperienced individuals or persons prone to adverse effects produces brief episodes of anxiety, panic, dysphoria, depression or mania disorders, depersonalization and misapprehension, bizarre and self-hetero aggressive behavior, delusions (in general, of a self-referential type) or hallucinations (more frequently visual).[4,16,22-24,29] Depending on the mixture of symptoms and behavior, these manifestations have been called acute panic reaction, toxic delirium, acute paranoid state or acute mania.[30] The disorder may occasionally start acutely (shortly after having finished a joint) or more slowly (1 to 2 hours) after the use of an oral dose, and usually remits completely in a few hours or a few days with no other treatment than a relaxing environment and the assurance, of people known to the subject, that the symptoms have been caused by marijuana (a "bad trip"). In addition, marijuana clearly worsens schizophrenia.[31] The reasons why cannabis is consumed by schizophrenics and the fact that cannabis may initially

cause a partial improvement of schizophrenic manifestations has been discussed. However, tolerance normally appears quite soon and according to the above-mentioned pattern. The subject increases the intake to ease the symptoms, which cause an increase in the so-called positive manifestations of schizophrenia, that is, delusions and hallucinations. This, in turn, leads to problems in several aspects of the individual's life, such as social conflicts (more self-hetero aggressiveness,[32]) increasing number of hospital admissions, ceasing treatment,[33] poorer response to psycho-pharmacological treatments.[34] All of these symptoms are signals of progressive deterioration in the disorder evolution in addition to indicating a poorer vital prognosis.[20]

It has also been reported that cannabis consumption worsens the prognosis of bipolar disorders; cannabis causes an increase of the phases or cycles, showing more severe manifestations and a precocious beginning of emotional symptoms.[35]

Adverse Mental Effects After Long-term Use

While there is a general consensus as far as the effects of marijuana are concerned, there is also broad disagreement concerning outcomes after prolonged use (more than 10 years).

Amotivational Syndrome

Chronic use of marijuana has been associated with a state characterized by apathy and loss of motivation, together with a decline in academic results and changes in behavior (known as "amotivational syndrome").[36] Very possibly, this syndrome could only result from the kind of intoxication typical in habitual consumers;[31] however, further research is necessary to validate this point.[37,38]

Cannabis Dependence?

Another aspect, widely discussed until recently, is whether cannabis consumption causes dependence. Signs and symptoms of abstinence appear in a few hours after giving up the drug, in subjects included in clinical studies.[39,40] An abstinence syndrome can witnessed after only 5 days of low but repeated doses for cannabis. In double blind studies with placebo[6] or THC use, the use of THC reduces the symptoms or causes them to disappear. Typical symptoms include: fatigue, diarrhea, insomnia, irritability, sweating, salivation, nausea, raised temperature, anorexia, weight loss, shivering, rebound disorder in the REM phase cycles, and subjective sleeping disorders. As a general rule, the symptoms disappear within 24 to 48 hours, but occasionally, sleeping disorders may last for weeks.

The first attempt to assess the degree of cannabis consumers' dependence has been carried out recently, through the use of a standardized questionnaire, the Marijuana Craving Questionnaire.[41] The questionnaire has proven to be a useful tool in the validation of cannabis abstinence syndrome.

Cognitive Deterioration

"The more consistent conductual effects of cannabis in humans are the alteration in memory functioning."[42] It is not clear what happens in individuals who have consumed cannabis on a daily basis, with 2 to 3 intakes per day, over a prolonged period of time. Research carried out on such individuals revealed a decrease in the performance on psychological tests measuring cognitive capacities (ie, memory).[43] The controversy arises at to whether the deterioration is reversible after stopping the intake of cannabis. Clinical trials performed with a small number of individuals have shown that they do recover a pre-morbid functioning standard after withdrawal symptoms.

The effects reappear once cannabis consumption is re-started,[44-46] although a subtle deterioration in certain cognitive capacities seems to occur, which is non-reversible after prolonged periods of withdrawal.[47]

Cannabis Psychosis

A psychotic condition with schizophrenic and manic symptoms, called "cannabic psychosis", which lasts for weeks or even months, has been described.[48] Its existence seems to have been confirmed by recent studies.[49] It may become chronic, if cannabis use is maintained. This happens when the consumer continues to take the drug in the hope that the substance will rid him of the symptoms he is suffering from.

Most criticism directed to denying the existence of the cannabic psychosis are best reflected by Thornicroft (1990) and Thomas (1993)[50,51] They refer to previous studies that focused mainly on the wrong patients, and did not use urinalysis tests, standardized interviews or control groups, etc. Since the 1990s, the vast majority of published studies[49,52-59] show major improvements in their methodology (selection of patients, use of urine analysis, and of standardized interviews, etc.), which make the results more trustworthy. In addition, the DSM-IV includes and epigraph entitled, "Cannabis induced psychotic disorder" in the chapter devoted to "Schizophrenia and Related Disorders."[60]

Nevertheless, the most recent bibliographic reviews[61-64] continue to doubt the existence of such a disorder, in the belief that it is no more than a first step towards full schizophrenia in subjects prone to it.[50,65]

Recently, a vulnerability model was applied to subjects who are cannabis consumers, in an attempt to explain why a previously healthy subject, who takes cannabis, continues to take it even though he has suffered from a psychotic disorder. Such pattern is known as "vulnerability-stress-coping"[66] and could be explained as follows: an individual starts using cannabis to overcome certain difficulties, which may be present in their daily activities; cannabis use increases the level of vulnerability towards the appearance of psychosis and, in turn, causes the appearance of a certain level of psychosocial stress, which together with cannabis use, causes schizophrenia to develop. Finally, the user continues to take the drug either hoping that cannabis will free him from the unpleasant feelings and perceptions caused by his illness (delirium, hallucinations, social isolation) or to minimize the effects that the pharmacological treatment.

LONG TERM EFFECTS

Effects on fetus of consuming mothers

Another aspect that we cannot overlook if the effect that cannabinoids have on the embryos of pregnant women. The results of research on animals show that a fetus which has been affected by their mothers' cannabis consumption, demonstrate important alterations in the homeostasis of several neurotransmitters (the most studied is dopamine) and their receptors.[67] Some of these alterations are not reversible. A similar Canadian study, carried out on humans,[68] demonstrated that there is a temporary alternation in the appearance of the alterations: after an initial period of up to 4 to 5 years, when failures in cognitive capacities can be observed; an "asymptomatic" period follows, which may continue for up to 11 to 12 years, after which the cognitive alterations reappear once more with additional problems including: lack of control of impulses, behavior disorders, and irritability.

Relationship between Cannabis and Schizophrenia

It seems quite clear that cannabis may trigger the appearance of schizophrenia.[16,22-24,69] Linzen et al[70] concludes that cannabis use is a risk factor in those individuals who show certain, specific, personality features or who have a family history of psychotic disorders; cannabis intake could lead these subjects to a chronic psychosis.

After the study by Andreasson[71] was widely criticized due to several faults in methodology, 3 new studies have been published, which show how cannabis intake is an etiopathogenic factor of schizophrenia.[72-74] These studies have not, as yet, been replicated, but the methodology used is very thorough and the results seem conclusive.

Affective Disorders (Mania or Depression)

Recent studies[75] have proven that cannabis not only worsens the evolution and prognosis of bipolar disorders, but also that its prolonged use may cause the appearance of such disorders or, at least, its precocious appearance.

A study by Patton et al[35] described the cases of young women who used cannabis frequently and after time, showed signs of depression and anxiety symptoms, with a frequency that is 5 times higher than those who do not consume cannabis. Arseneault et al[74] also found similar results, with an increase not only of the manifestations, but also in the depression syndrome. Rey and Tennat[76] share this opinion.

Gateway Drug

Whereas the most recent studies have contributed to the clarification of each one of the previously discussed issues, this is not true concerning the question of cannabis as a gateway drug. In 1999, the Institute of Medicine concludes that the data provided by the different studies carried out up to that time, were not enough to adopt a clear position; the only clear conclusion was that in most cases, cannabis consumption just precedes the use of other drugs (except tobacco and alcohol) but does not appear to be the cause of consuming other drugs.[38] The only trustworthy prediction was the relation between the high consumption of cannabis and the presence of a co-morbid psychiatric pathology.[77]

The latest studies continue to show conflicting results: Fergusson and Horwood[77] conclude that cannabis may act as a gateway drug; Beenstock and Rahav[79] conclude that their evidence does not back up the hypothesis that the use of cannabis leads to the consumption of other drugs. Morral et al[80] contribute the hypothesis that there is a general tendency among consumers towards the consumption of any substance, not only cannabis (Common-factor model), which explains why it is not necessary to turn to the hypothesis of the gateway effect of cannabis to justify users shifting from one substance to another.

CONCLUSION

Cannabis is the most consumed illegal drug in the western world and it has the image of a soft drug that is not very dangerous among most of its users. However, there are many potential dangers in its indiscriminate use, not only mental, but also physical. Some of the effects are irreversible (ie, cognitive deterioration, appearance of schizophrenia, etc.), even in cases where cannabis use is ceased. Although it is also true that in the vast majority of these cases, those consequences appear after prolonged consumption.

All of this is occurring at a time when there is an increase both in the number of cannabis users and in the percentage of THC per use, which

increases the risk of suffering undesirable psychological effects. At the same time, research on humans has intensified, in order to assess canabinoids' safety as therapeutic agents. The adverse effects discussed should not be overlooked when debating the pros and cons of legalization of cannabis.

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