

REVIEW ARTICLE

Cannabis and anxiety: a critical review of the evidence

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Background Anxiety reactions and panic attacks are the acute symptoms most frequently associated with cannabis use. Understanding the relationship between cannabis and anxiety may clarify the mechanism of action of cannabis and the pathophysiology of anxiety. Aims of the present study were to review the nature of the relationship between cannabis use and anxiety, as well as the possible clinical, diagnostic and causal implications.

Method Systematic review of the Medline, PsycLIT and EMBASE literature.

Results Frequent cannabis users consistently have a high prevalence of anxiety disorders and patients with anxiety disorders have relatively high rates of cannabis use. However, it is unclear if cannabis use increases the risk of developing long-lasting anxiety disorders. Many hypotheses have been proposed in an attempt to explain these relationships, including neurobiological, environmental and social influences.

Conclusions The precise relationship between cannabis use and anxiety has yet to be established. Research is needed to fully clarify the mechanisms of such the association. Copyright © 2009 John Wiley & Sons, Ltd.

KEY WORDS — Cannabis sativa; tetrahydrocannabinol; cannabidiol; anxiety; psychosis

INTRODUCTION

Association between *Cannabis sativa* and psychopathologic conditions have existed since before the Christian era (Zuardi *et al.*, 2006). However, while there has been considerable interest in the relationship between cannabis use and psychosis (Arseneault *et al.*, 2004), the association between cannabis and other psychiatric disorders, particularly anxiety, has received relatively little attention. One of the possible reasons is that patients with cannabis-associated anxiety do not attract as much attention from clinical services as those

with psychosis. As the drug is illegal in most countries, patients with anxiety may be reluctant to reveal cannabis use (Degenhardt *et al.*, 2003). Moreover, anxiety may be induced by cannabis use or may be a symptom of withdrawal in the context of cannabis dependence, the existence of which has been a matter of debate (Budney *et al.*, 2004; Rosenberg and Anthony, 2001). Thus this may result in confusion about the diagnosis of anxiety symptoms reported in the context of recent cannabis use. Understanding the association between cannabis use and anxiety may clarify both the mechanism of action of cannabis and the pathophysiology of anxiety. Given that cannabis is the most widely used illicit drug in the world (Murray *et al.*, 2007) and anxiety is the most prevalent mental disorder (Kessler *et al.*, 2005), these are issues of great interest.

The purpose of this critical review was to investigate the nature of relationship between cannabis use and anxiety, as well as the possible clinical, diagnostic and causal implications.

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METHODS

We performed systematic searches of the following electronic databases to identify all studies published in the English language from their inception to August 2008: Medline, PsycLIT and EMBASE. The search terms used were CANNABIS, MARIJUANA, THC, TETRAHYDROCANNABINOL, DELTA-9-TETRAHYDROCANNABINOL, CANNABINOIDS and ANXIETY, PANIC, PHOBIA and STRESS. Where Medical Subject Heading terms were available, they were enlarged and incorporated. The reference lists of eligible papers were checked for additional relevant studies.

RESULTS

Vulnerability and acute effect

Cannabis can cause an acute and short-lasting episode of anxiety, which often resembles a panic attack, in those who are not habitual users. When taken in high doses [(>5 mg oral Δ^9 -tetrahydrocannabinol (Δ^9 -THC) for a man of average weight], cannabis can cause intense fear and anxiety. With higher doses, panic and phobic attacks may occur (Hall and Solowij, 1998; Roy-Byrne and Uhde, 1988; Thomas, 1993; Tournier *et al.*, 2003; Tunving, 1987). About 20–30% of users show brief acute anxiety reactions after smoking the drug (Hollister, 1986; Thomas, 1996). Such symptoms usually occur when the drug is used at high doses and are more common in drug-naïve subjects and in novel or stressful environmental situations (Manzanas *et al.*, 2004).

This has been consistently described in experimental studies in man (D'Souza *et al.*, 2004; Gregg *et al.*, 1976; Naliboff *et al.*, 1976; Zuardi *et al.*, 1982) and in many case reports (Deas *et al.*, 2000; Moran, 1986). Such manifestations mostly resemble those described in patients with anxiety disorders.

Anxiety reactions and panic attacks appear to result in aversion to further use of the drug, as these symptoms are one of the most common reasons given for the cessation of cannabis use. These individuals are also less likely to become regular users (Thomas, 1996). Similarly, cannabis can exacerbate existing anxiety symptoms, precipitate recurrence of an acute episode and counteract the effects of anxiolytic medication (Szuster *et al.*, 1988). Table 1 summarises the factors associated with the risk of anxiety induced by cannabis use.

Table 2 summarizes the experimental studies involving acute administration of cannabinoids on human anxiety.

Table 1. Factors associated with the risk of anxiety induced by cannabis use

Individual and genetic vulnerability
Personality traits
Gender
Frequency of use
Dose and quantity consumed
Proportions and concentration of cannabinoids ^a
History of previous episode
Presence of anxiety disorders/symptoms
Basal anxiety levels
Abstinence states
Environment and context of use

^aEspecially of Δ^9 -tetrahydrocannabinol (Δ^9 -THC) and cannabidiol (CBD).

In contrast, long-term users typically report that cannabis use is associated with a *reduction* in anxiety. Relaxation and relief from tension remain the most common effects of using cannabis and the most common reasons for using the drug (Boys *et al.*, 1999; Hathaway, 2003; Reilly *et al.*, 1998).

Evidence of the association between anxiety and cannabis use

Cannabis use and anxiety symptoms. Frequent cannabis users appear to have higher levels of anxiety than non-users, without these necessarily representing an anxiety disorder. In a study with people who regularly used cannabis for at least 10 years, 21% of the subjects had high levels of anxiety (Reilly *et al.*, 1998). In another study involving draftees to the Italian army, it was found that the severity of anxiety symptoms increased progressively with increasing cannabis use and higher levels of anxiety were observed in those who reported abuse or dependence on the drug (Troisi *et al.*, 1998). A recent study confirmed that cannabis dependence in adolescents is related to increased psychological distress and anxiety levels (Dorard *et al.*, 2008). A similar result was found in two indigenous communities in the northern territory of Australia (Clough *et al.*, 2005). The authors found that the severity of symptoms within the 'anxiety-dependency' cluster in cannabis users increased as their level of cannabis use increased (Clough *et al.*, 2005). This seems to be particularly evident among women, as observed in cannabis-dependent individuals arrested for marijuana-related offending behaviour (Feeney *et al.*, 2005). State anxiety level was also one of the main predictors of increased severity of cannabis use (Spalletta *et al.*, 2007), while the marijuana use increased the risk for anxiety symptoms and catastrophic thinking (Zvolensky *et al.*, 2006b). Furthermore, a recent

Table 2. Acute effects of cannabinoids in experimental studies on human anxiety

Study	Subjects (N)	Cannabinoid	Route	Dose	Results
Anxiogenic effect					
Karniol <i>et al.</i> (1974)	40	Δ^9 -THC	Oral	30 mg	Reported anxiety and panic
Gregg <i>et al.</i> (1976)	10	Δ^9 -THC	Intravenous	0.022 and 0.044 mg/kg	Intensify scores of STAI ^a during oral surgery
Naliboff <i>et al.</i> (1976)	15	Δ^9 -THC	Inhalatory (cigarettes)	14 mg	Intensify FBF ^b and HR ^c means during arithmetic task
Peters <i>et al.</i> (1976)	10	Δ^9 -THC	Oral	0.2, 0.4 and 0.6 mg/kg	Increased scores of tension items of SDEQ ^d
Zuardi <i>et al.</i> (1982)	8	Δ^9 -THC	Oral	0.5 mg/kg	Increased scores of STAI ^a
D'Souza <i>et al.</i> (2004)	22	Δ^9 -THC	Intravenous	2.5 and 5 mg	Increased anxious scores of VAS ^e
Ilan <i>et al.</i> (2005)	23	Δ^9 -THC	Inhalatory (cigarettes)	3.6%	Increased anxious scores of VAS ^e
Fusar-Poli <i>et al.</i> (2009)	15	Δ^9 -THC	Oral	10 mg	Increased scores of STAI ^a
No effect					
Glass <i>et al.</i> (1980)	4	Nabilone	Oral	1 and 4 mg	No significant effect on POMS ^f anxiety
Ilan <i>et al.</i> (2005)	23	Δ^9 -THC	Inhalatory (cigarettes)	1.8%	No significant effect on VAS ^e anxious scores
Anxiolytic effect					
Karniol <i>et al.</i> (1974)	40	CBD	Oral	15, 30 and 60 mg	Reported less anxiety and panic induced by Δ^9 -THC
Zuardi <i>et al.</i> (1982)	8	CBD	Oral	1 mg/kg	Decreased STAI ^a scores elevation induced by Δ^9 -THC
Zuardi <i>et al.</i> (1993)	10	CBD	Oral	300 mg	Decreased VAS factor anxiety scores after public speaking
Crippa <i>et al.</i> (2004)	10	CBD	Oral	400 mg	Decreased VAS factor anxiety scores before SPECT ^g procedure
Fusar-Poli <i>et al.</i> (2009)	15	CBD	Oral	600 mg	Decreased skin conductance fluctuation in task with fearful face

^aState-Trait Anxiety Inventory.

^bForearm Blood Flow.

^cHeart Rate.

^dSubjective Drug Effects Questionnaire.

^eVisual Analog Scale.

^fProfile of Mood States.

^gSingle-Photon Emission Computed Tomography.

study in university students indicated that the association between cannabis use and anxiety symptoms may trigger risky and suicidal behaviours (Innamorati *et al.*, 2008).

Comorbidity between cannabis use and anxiety disorders. Comorbidity is defined as the overlap of two or more psychiatric disorders. In general, few epidemiologic studies have evaluated the comorbidity of cannabis use and anxiety in the general population. These studies have suggested that chronic cannabis use is associated with a higher prevalence of comorbidity with anxiety disorders, especially panic and social anxiety disorders.

In a study with 18-year-old New Zealanders, it was reported that those who had consumed cannabis ten times or more between the ages of 15 and 16 had a higher prevalence of anxiety disorders (31%) – more than twofold that of individuals who had never used the drug (Fergusson and Horwood, 1997).

Analysis of data obtained in the National Comorbidity Survey (NCS) suggested that the probability of diagnosing anxiety or mood disorder (either in the

previous month or throughout life) was approximately doubled in subjects with cannabis dependence. Thus, subjects with cannabis dependence had a higher comorbidity with anxiety disorders (between 6.9 and 29%, depending on the disorder) than those without cannabis dependence. It was also observed that a considerable number of subjects developed anxiety disorders before the first symptoms of cannabis dependence suggesting that some of them may have been using cannabis as a self-prescribed anxiolytic medication (Agosti *et al.*, 2002). In line with this hypothesis a recent study observed that social anxiety disorder is an independent risk factor for cannabis dependence (Buckner *et al.*, 2008).

In a study by the Australian National Survey of Mental Health and Well-Being, in subjects aged over 18, it was verified that 17% of individuals with cannabis dependence showed anxiety disorders compared to only 5% of non-users. Nonetheless, cannabis use did not appear to be related to anxiety when the data was adjusted for demographic characteristics, other substance use and personality traits (Degenhardt *et al.*, 2001).

Subsequently, it was also observed that agoraphobia is significantly associated with higher predisposition to cannabis use, regardless of anxiety condition and other confounding factors. However, the authors did not find evidence of anxiolytic or anxiogenic effects in daily cannabis use (Tournier *et al.*, 2003).

A lifetime history of cannabis dependence has been significantly related to an increased risk of panic attacks. In addition, the authors of this study found that the age of onset of panic attacks was significantly earlier among the subjects with both conditions than for individuals with panic attack with no cannabis use (Zvolensky *et al.*, 2006a). Another recent prospective longitudinal study investigating 1709 adolescents showed that cannabis use and dependence were significantly associated with an increased risk for the development of panic attacks and panic disorder (Zvolensky *et al.*, 2008).

As occurs with other illicit drugs, individuals with anxiety disorder have a stronger chance of presenting with cannabis dependence or abuse throughout life and *vice versa*. For example, Strike *et al.* (2003) verified that 13% of individuals dependent on cannabis who sought treatment had a history of previous anxiety disorder. Similarly, Swadi and Bobier (2003) verified that 63% of patients hospitalized with an anxiety disorder presented with a comorbid substance abuse disorder, especially cannabis. On the other hand, suffering from an anxiety disorder seems to be one of the most important reasons for cannabis users to seek psychiatric treatment.

Anxiety as manifestation of cannabis abstinence. Anxiety is one of the main manifestations of the cannabis withdrawal syndrome (Bonn-Miller *et al.*, 2007; Haney, 2005). Its onset is typically between the second and sixth day and lasts from 4 to 14 days (Budney *et al.*, 2004). The severity and duration of these effects are comparable to those of tobacco and other withdrawal syndromes, which commonly contribute to the development of dependence and difficulty in abstinence (Vandrey *et al.*, 2005). However, the existence of a cannabis withdrawal syndrome is not universally accepted and it is still not included in the DSM-IV (American Psychiatric Association, 1994).

Bupropion and Divalproex have not proven effective in treating cannabis withdrawal symptoms (Haney *et al.*, 2001, 2004). In another single dose study, Nefazodone effectively decreased some marijuana withdrawal symptoms, but did not affect the majority of the symptoms (Haney *et al.*, 2003). The most promising demonstration of suppression of symptoms of cannabis withdrawal was observed through the use

of oral Δ^9 -THC (from 30 to 90 mg/day), which decreased both symptoms and cravings. At this dose it did not produce intoxication and induced only minimal adverse effects (Budney *et al.*, 2007; Haney *et al.*, 2004).

Cannabis use and risk for developing anxiety disorders. While there is little doubt that cannabis use can cause anxiety symptoms, it is less clear that it can increase the risk of developing anxiety disorders which persist after the cessation of use. Several cases of agoraphobia (Moran, 1986) and panic disorder (Dannon *et al.*, 2004; Langs *et al.*, 1997) induced by cannabis use have been previously described. Some authors have also speculated that cannabis use may be associated with enduring anxiety symptoms, as these clinical observations parallel data from animal studies (O'Shea *et al.*, 2004, 2006).

It was observed that frequent cannabis use in adolescent females doubled the chances of their subsequently presenting with anxiety and depressive conditions, with daily cannabis use increasing the risk fourfold (Patton *et al.*, 2002). As depression did not predict higher cannabis use in later life, this seems unlikely to reflect self-medication with cannabis for these symptoms; consistent with an earlier report (McGee *et al.*, 2000). These findings have been replicated by a recent study which followed up a cohort of 3239 Australian young adults from birth to the age of 21 years. After controlling for confounding factors, those who started using cannabis before the age of 15 years and used it frequently at 21 years were more likely to report symptoms of an anxiety disorder in early adulthood (Hayatbakhsh *et al.*, 2007). However, contrasting results were observed in a large longitudinal study that focused on the vulnerability factors in adolescent substance use (Windle and Wiesner, 2004). These contrasting findings were further supported by a recent study which investigated whether cannabis use predicted the first incidence of mood and anxiety disorders in 6000 adults during a 3-year follow-up period. Use of cannabis at baseline predicted a modest increase in the risk of a first episode of major depression and a stronger increase in the risk of a first episode of bipolar disorder. Although there was an association noted between cannabis use and anxiety disorders, it did not survive after controlling for confounding factors (Van Laar *et al.*, 2007).

Given that the relationship between anxiety symptoms and cannabis use in individuals with comorbid cannabis use and anxiety disorders is clinically complex and they normally continue to use the drug,

there is a growing concern that they may be difficult to treat. Thus, Dannon *et al.* (2004) studied several patients with panic disorder, the onset of which began 48 h after cannabis use. The authors found that such cases were responsive to pharmacological treatment with paroxetine. However, it was recently observed that the combination of cognitive-behavioural therapy and pharmacotherapy was not effective for the treatment of panic or social phobia symptoms among occasional cannabis users (Bricker *et al.*, 2007).

Nonetheless, the existence of a causal relationship between cannabis use and long-term anxiety disorders remains dubious (Gilder *et al.*, 2006; Windle and Wiesner, 2004). For instance, if cannabis use were to have been responsible for the precipitation of anxiety disorders, one would have expected an increase in the number of people presenting with these disorders in recent years, as the prevalence and extent of cannabis use has increased in recent times (Boydell *et al.*, 2006; Iversen, 2003).

Possible explanations for the association between anxiety and cannabis use

In spite of some studies suggesting that there exists an association between cannabis use and high levels of anxiety, personality traits and anxiety disorders, they are not informative regarding the parameters of such association (Compton *et al.*, 2000; McGee *et al.*, 2000; Meser *et al.*, 1998). Many hypotheses have been proposed in an attempt to explain this relationship.

How could cannabis modulate anxiety? Using cannabis could precipitate acute anxiety in two ways:

- (i) The main active psychoactive ingredient in cannabis, Δ^9 -THC, could elicit anxiety symptoms through its effects on serotonin, noradrenalin (Braida *et al.*, 2007; Degenhardt *et al.*, 2003; Muntoni *et al.*, 2006) GABA and glutamate (Pertwee, 2008). Although there is relatively scarce information about the interactions between the serotonergic and the endocannabinoid systems, there is some emerging evidence of a complex interplay between the two systems, the full extent of which is not yet clear (Braida *et al.*, 2007; Viveros *et al.*, 2005). Recent animal studies have confirmed that cannabidiol (CBD), the non-psychotomimetic constituent of *Cannabis sativa* plant that induces anxiolytic effects may do so by having an effect on 5HT_{1A} receptors (Braida *et al.*, 2007; Campos and Guimarães, 2008; Patel and Hillard, 2006; Witkin *et al.*, 2005).
- (ii) Acute intoxication could also lead to anxiety secondary to impaired cognitive functioning and the clouding of consciousness.

In mice and rats, administration of Δ^9 -THC causes stronger aversion to the open arms on the elevated plus-maze, similar to the effect of anxiogenic agents (Moraes and Lutz, 2008; Onaivi *et al.*, 1990). Conversely, CBD, when administered with THC at therapeutically relevant ratios, ameliorate aversive effects associated with initial use of THC alone (Vann *et al.*, 2008).

Cannabis use could also lead to persisting anxiety disorders through an enduring deregulation of the endocannabinoid systems (anandamide), particularly in genetically vulnerable individuals (Witkin *et al.*, 2005). Additionally, emerging data from human and animal perinatal exposure studies suggest neurodevelopmental or hormonal effects of cannabis upon subsequent anxiety and mood states, especially among adolescents (Sundram, 2006).

Similarly, there could be other indirect relationships. For instance, chronic cannabis use beginning at a young age could increase the possibility of lower educational attainment levels due to dropouts or failure. This could limit employment prospects and subsequent unemployment could increase stress resulting in anxiety symptoms/disorders (Lynskey *et al.*, 2002). Other psychosocial mechanisms, such as the adoption of a countercultural lifestyle, may also underlie the association (Patton *et al.*, 2002). Moreover, in respect to panic disorder, it was postulated that cannabis withdrawal symptoms might increase the chance of panic-relevant learning, as individuals experience more intense interoceptive sensations and misinterpret them as personally dangerous, potentially leading to a panic attack (Zvolensky *et al.*, 2006a, 2008).

Anxiety leads to cannabis consumption. Prospective studies indicated that anxiety disorders in adolescence may predict later cannabis use and cannabis use disorder (Wittchen *et al.*, 2007). The most popular explanation for this relationship is that subjects with high levels of anxiety and patients with anxiety disorders use cannabis as a form of 'self-medication' (Arendt *et al.*, 2007; Stewart *et al.*, 1997). Supporting this idea, many subjects report using cannabis to relax, to cope with stress and as a way to reduce anxiety (Bonn-Miller *et al.*, 2007; Boys *et al.*, 1999; Buckner *et al.*, 2008; Hathaway, 2003; Osborne *et al.*, 2000; Reilly *et al.*, 1998). Moreover, the expectation that cannabis will reduce anxiety has been associated with its use in non-clinical undergraduates as well as in psychotic subjects (Schofield *et al.*, 2006) and in their relatives (Smith *et al.*, 2008) as well as in individuals with HIV/AIDS (Prentiss *et al.*, 2004; Woolridge *et al.*, 2005), among other conditions.

This hypothesis has been partially supported by data from a study in which the anxiolytic effects of Nabilone (3 mg/day), a synthetic cannabinoid derived from Δ^9 -THC, were evaluated. In a double-blind, placebo-controlled study, patients with anxiety disorders demonstrated reduced symptoms after 28 days of treatment with nabilone (Fabre and McLendon, 1981). Ilaria *et al.* (1981) in a placebo-controlled cross-study, also verified the ability of nabilone (2–5 mg/day) to reduce symptoms of anxious patients as assessed by the Hamilton Anxiety Scale. Nevertheless, it is prudent to discourage using cannabis, particularly in patients with psychosis or anxiety disorders.

Common factors increase risk for anxiety as well as for cannabis use. In this model, both anxiety disorder and cannabis use could have common etiopathological causes. Such factors include biological, neurodevelopmental, environmental and social influences, as well as personality traits or a combination of all of them (Chabrol *et al.*, 2005; Lynskey *et al.*, 2002; Windle and Wiesner, 2004). For example, animal studies have indicated that maternally deprived adolescent rodents have altered responses to cannabinoid compounds (Marco *et al.*, 2008). Other investigations have suggested that perinatal THC exposure induced an anxiogenic-like profile in the adult offspring tested in the elevated plus-maze test (Trezza *et al.*, 2008). Similarly, factors associated with substance abuse in patients with anxiety disorders appear to be similar to those associated with substance abuse in the general population (i.e. cost, availability, boredom, impulsiveness, seeking sensation and facility of social interaction, among others) (Bonn-Miller *et al.*, 2007; Sbrana *et al.*, 2005). For instance, peer influence may have a role in problematic cannabis use even among individuals with social anxiety disorder (Buckner *et al.*, 2006).

Cannabis use by patients with anxiety disorders could also reflect a specific genetic vulnerability. For instance, both psychotic subjects and their relatives have been shown to present high rates of cannabis use (Smith *et al.*, 2008). Alternatively, genetic factors could increase risk for anxiety in cannabis users, especially male subjects (Schofield *et al.*, 2006).

CONCLUSION

It is paradoxical that while individuals report reduced anxiety as the motivation for using cannabis, yet acute anxiety is the most common adverse effect of cannabis use. These conflicting statements may be reconciled through the observation that the effects of cannabis on

anxiety appear to be dose-dependent. Thus, low doses of the cannabinoid receptor agonists, nabilone (Onaivi *et al.*, 1990), CP 55,940 (Marco *et al.*, 2008) and Δ^9 -THC (Berrendero and Maldonado, 2002) have anxiolytic-like effects in laboratory rodents, whereas higher doses produce anxiogenic behaviour and activate the hypothalamic–pituitary–adrenocortical axis (Berrendero and Maldonado, 2002; Giuliani *et al.*, 2000; Manzanares *et al.*, 1999; Viveros *et al.*, 2005). Anxiety induced by Δ^9 -THC is facilitated by exposure to novel or stressful environments that appears to be mediated by the central amygdala (Patel *et al.*, 2005; Phan *et al.*, 2008).

Although Δ^9 -THC is commonly regarded as the main factor responsible for the psychoactive effects of cannabis, several reports have demonstrated that other components of the plant influence its pharmacological activity. One of these compounds is CBD, which may constitute up to 40% of cannabis extracts and is not associated with the psychological and cognitive effects usually associated with cannabis use in humans. In fact, studies in laboratory animals and in humans have demonstrated that CBD has anxiolytic properties (Fusar-Poli *et al.*, 2009); in contrast with the anxiogenic effects of Δ^9 -THC in high doses (Zuardi *et al.*, 1982). Plant samples vary in the proportions and relative concentrations of THC and CBD. These depend on soil and weather conditions, where the plant grew, the part of the plant which provided the sample (stems have more CBD, leaves and flowers have more Δ^9 -THC); and other factors.

The present review demonstrates that cannabis use and anxiety symptoms/disorders often co-occur. Several factors may explain this association, but further research is needed to clarify the mechanisms by which cannabis use may cause acute anxiety and long-lasting anxiety disorders. Longitudinal studies may be helpful in obtaining better understanding of environmental, social, neurobiological and other confounding factors. Through such studies, more specific and efficacious treatments and primary prevention strategies could be more easily developed.

CLINICAL IMPLICATIONS

- Anxiety is the acute symptom most frequently associated with cannabis use, particularly at high doses. Acute anxiety following cannabis use is more common in drug-naïve subjects and when the drug is taken in novel or stressful environments.
- Cannabis use alone does not appear to be sufficient or necessary for the development of long-term anxiety but

may be a risk factor that operates in conjunction with other vulnerability factors.

- Chronic cannabis use is associated with higher prevalence of anxiety disorders and *vice versa*. In addition, acute anxiety can be a feature of a cannabis withdrawal syndrome.

LIMITATIONS

- While several environmental, social and neurobiological factors have been implicated in the association between cannabis use and anxiety, the precise basis of the relationship remains unclear.
- Only a few prospective studies have been conducted and these have relied on self-reported measures of cannabis use.
- More longitudinal studies are required to estimate the long-term impact of cannabis use on anxiety and anxiety disorders.

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