6 Cannabis and depression: What does the research say?

The first medicinal use of cannabis in the Western world was as an antidepressant and there have been case reports of patients with depression that have shown a better response to cannabis than to conventional antidepressants. The otherwise counterintuitive report of cannabis also reducing mania is consistent with the hypothesised stabilising influence of the endocannabinoid system. However, heavy cannabis use has been associated with depression.

The USA and Australia have conducted national surveys that have assessed the level of various mental health disorders in the population in recent years. In Australia, data from the National Survey of Mental Health and Well-being was used by Degenhardt and colleagues to assess the relationship between depression and cannabis use. A positive relationship was found between cannabis use and depressive disorders, and this relationship became stronger with heavier or more problematic cannabis use. However, once other drug use was controlled for—particularly alcohol and tobacco—the relationship did not remain significant. The authors concluded that there was no direct relationship between cannabis use and depression, but acknowledged that there may be an indirect one such that cannabis users are more likely to be dependent on other drugs, which may in turn increase the risk of depression. As an avoidant coping style, which includes using drugs, is associated with depression, this is a plausible explanation.

Agosti and colleagues used the data from the United States National Comorbidity Survey to assess the prevalence of psychiatric disorders among those with cannabis dependence. They found that the vast majority (90%) of cannabis-dependent respondents also had a lifetime mental health disorder, compared to just over half of those without cannabis dependence. Cannabis-dependent respondents were over twice as likely to have ever experienced clinically-significant depression as those who were not dependent on the drug. Furthermore, those who were currently using cannabis were still twice as likely to have a current mood disorder as those who had never been dependent on cannabis.

Further analysis of the United States National Comorbidity Survey data showed that, although history of cannabis use and cannabis dependence were associated with an increased risk of experiencing an episode of clinically-significant depression, this risk was moderate and was not greater than the risk of depression associated with being female or a tobacco smoker. Among Canadian adolescents, cannabis use has been found to be an independent risk factor for depression. Risk was analysed in the former study by taking into account the age of first cannabis use and the age of first episode of depression and in the latter study by an instrument designed to measure depression risk. However, these are not ideal methods for evaluating whether cannabis is a causal factor for depression as the studies were cross-sectional.

Prospective studies are required to determine whether there is an association between cannabis and depression and, if so, to assess its causal structure. Until quite recently, there was a lack of prospective cohort studies assessing the relationship between cannabis...
and depression, and reviews were unable to make firm statements about the nature of the relationship [200]. In the last few years, a number of studies have been released that assess whether cannabis use predicts depression [18][21][21][62]. These as well as earlier studies are reviewed below.

6.1 Major cohort studies on cannabis and depression: A review of the findings

6.1.1 Christchurch Health and Development Study

Fergusson and Horwood [212] assessed early cannabis use and subsequent psychosocial outcomes among a birth cohort in New Zealand and found that the rates of experiencing an episode of clinically-significant depression between the ages of 16 and 18 years were significantly higher for those that had used cannabis between the ages of 15 and 16 than those who had not used the drug. However, once confounding variables were controlled for, this association was not significant. The variables that were controlled included: coming from a socially disadvantaged background; having adverse experiences in childhood; associating with deviant peers; and having poor parental attachments.

A more recent study of the same birth cohort found that cannabis use was associated with depression, suicidal ideation (i.e. having thoughts of taking one’s own life) and attempting to take one’s own life, particularly those who used cannabis at least weekly [213]. Weekly cannabis users between the ages of 14 and 15 were at greater risk of suicidal ideation and attempt than weekly cannabis users who were 20 to 21 years of age. The birth cohort design allowed for a variety of confounding factors to be controlled for, including adverse life events, deviant peer affiliations, alcohol abuse, age of leaving school and age of leaving home. After adjusting for these factors, weekly cannabis users at all ages were almost twice as likely to experience depression. Those aged 14 to 15 years were over seven times more likely to have thoughts of ending their life and thirteen times more likely to have attempted to take their own life (confidence intervals were not reported). However, because this particular study was looking at the association between cannabis use and depression/suicide outcome at the same age, it could not be determined whether cannabis use preceded depression, or depression preceded cannabis use.

6.1.2 Epidemiological Catchment Area (EPA) Study

The EPA study is a multisite survey of the adult US population. Participants from one of these sites (Baltimore) were followed up 14–16 years after baseline assessment, to determine whether cannabis abuse predicted later development of depressive symptoms [214]. After adjusting for confounders, it was found that those who abused cannabis at baseline were four times more likely to experience at least one depressive symptom (including thoughts of ending their life and inability to experience pleasure) 14–16 years later. The converse relationship did not exist; depressive symptoms at baseline did not predict follow-up cannabis use.
6.1.3 Children in the Community Study

Another study from the United States followed a community sample of children aged between one and ten years until their late twenties [215]. After control of confounding factors (demographic factors, socioeconomic status and prior episodes of major depressive disorder and substance use disorders) it was found that childhood cannabis use (prior to the age of about 14 years) was associated with a modestly increased risk of MDD in the late twenties, compared to those who had not used cannabis. The association between adolescent cannabis use and later MDD was similar (see Table 6.1). However, the association between cannabis use in the early twenties was not associated with later MDD.

6.1.4 Lives Across Time Study

The Lives Across Time: A Longitudinal Study of Adolescent and Adult Development (LAT) study commenced in 1988 with the aim of measuring the effect of alcohol and cannabis use by adolescents on subsequent functioning by the cohort. Among other measures, cannabis use was measured at four points (15.5 to 17.5 years) near the average age of initiation of cannabis use. Marijuana use trajectories were used to stratify the sample into abstainers, decreasers, experimental users, high-chronics and increasers on the basis of the pattern of use over the two years of adolescent use measured. While increasers (those whose marijuana use increased greatly from 15.5 to 17.5 years) scored higher on the CES-D than abstainers as adolescents, this effect was not significant at the young adult (about 23.5 years) assessment. Notably, increased depression scores were not observed in the high-chronic group at either assessment.

6.1.5 Victorian Adolescent Health Cohort Study

The Victorian Adolescent Health Cohort Study is a cohort study which has been following a group of Australian adolescents since 1992, when they were in Grade 9 or 10 (approximately 14 or 15 years old). Patton and colleagues [216] reported that frequent cannabis use (weekly or more) during adolescence predicted adult depression and anxiety in females, even after controlling for confounding variables such as adolescent depression and anxiety, antisocial behaviour, alcohol use, parental separation and parental education. There was no relationship between depression and anxiety in adolescence and use of cannabis in adulthood. It should be noted that other illicit drug use was not controlled for.

6.1.6 Dunedin multidisciplinary health and development study

A study using data from this New Zealand birth cohort found that late-onset cannabis use (at age 18) was associated with depression at age 26, but early-onset cannabis use (by age 15) was not, once other drug use, gender and socioeconomic status were controlled for [12]. Cannabis use (later or early onset) was not associated with depressive symptoms.

6.1.7 National Longitudinal Survey of Youth

The National Longitudinal Survey of Youth is an American longitudinal survey that has been running since 1979. A recent study investigated the association between cannabis use and depression among this cohort once they had reached adulthood [210]. When members of the cohort were assessed in 1994 (when they were aged between 29 and 37 years), the
prevalence of depression was greater among those who had used cannabis during the past year (23%) than those who had not used cannabis (17%). However, after adjusting for a range of potential confounders (age, gender, ethnicity, general health, region of residence, criminal activity, educational achievement, socioeconomic status, depression before cannabis use, and other substance use), cannabis use in the past year was not significantly associated with depression. The researchers also analysed whether heavy cannabis use in the past year was associated with depression, and whether cannabis use in 1998 was associated with depression four years later. The odds ratios associated with these were not significant either. The researchers concluded that associations between cannabis use and depression may be attributable to common factors related to depression and the decision to use cannabis.

6.1.8 National Longitudinal Study of Adolescent Health

This is an American school-based survey that assessed high school students (mean age 15) on a number of variables at baseline and one year later [217]. Although cross-sectional relationships existed at each assessment, after controlling for a number of variables (see table 6.1), there was no relationship between cannabis use at baseline, and depression at follow-up. There was also not a relationship between depression at baseline and cannabis use at follow-up.

6.1.9 Ontario Child Health Study

The Ontario Child Health Study is a prospective study of a cohort of adolescents, aged between 12 and 16 at baseline, followed up after four years and eight years. A very recent study assessed the relationship between adolescent and adult cannabis use, defined as any use in the last six months (adolescence) or 12 months (adulthood), and depression in adulthood, defined as diagnosis of major depressive disorder in the previous 12 months [211]. It was found that those who used cannabis in adolescence, but did not continue to use in adulthood, were not at an increased risk of adult depression, after control of confounding factors assessed in adolescence (socioeconomic status, single parent home, family functioning, gender, age, grade failure, health status, externalising syndromes—such as behavioural problems, and internalising syndromes—such as depression and anxiety). However, those who used cannabis in adulthood but not in adolescence were over twice as likely to experience depression in adulthood, and adult cannabis users who began using cannabis during adolescence were over four times as likely to experience depression.

6.1.10 The Mater University Study of Pregnancy (MUSP)

The Mater University Study of Pregnancy (MUSP) is a birth cohort study commenced in 1981. One aim was to assess the association between cannabis use and anxiety and depression [62]. Anxiety and depression were measured together using the Youth Self-Report questionnaire at the age of 14 and the Young Adult Self-Report version of the Child Behaviour Checklist at the age of 21. Frequency of cannabis use during the past months was assessed at age 21, as well as the age of first use. Participants were considered ‘early onset cannabis users’ if they reported using cannabis at age 14 or younger. It was found that those who used cannabis frequently were about twice as likely to have symptoms of anxiety and depression, and about three times as likely if cannabis use had been
initiated at age 14 or earlier. These associations were found after controlling for a variety of socio-demographic factors, alcohol consumption, smoking and mental health disorders. Additionally, a relationship still existed between cannabis use and anxiety and depression even when no other illicit drugs had been used. No association was found between symptoms of anxiety and depression at age 14 and use of cannabis at age 21.

6.1.11 Cannabis and suicide risk

The studies reviewed so far have mainly focused on depressive symptoms or diagnosis of a major depressive disorder. However, some also assess the relationship between cannabis use and suicidal behaviour. The Christchurch study found that cannabis use was associated with increased risk of thoughts of suicide and attempting suicide, particularly for younger people [213]. Suicidal ideation was one of the depressive symptoms that were predicted by cannabis use in the Epidemiological Catchment Area study from the United States [214]. Another study from the United States assessed risk for suicide among a group of school children (n=1695) in early adolescence, late adolescence and adulthood [218]. Females who began using cannabis in early adolescence were almost three times more likely than females who did not do so to have suicidal thoughts in adulthood. In the National Longitudinal Study of Adolescent Health [219], cannabis use was found to be a risk factor for suicide attempts, but a number of confounding variables were not controlled for, and the follow-up period was short (11 months).
<table>
<thead>
<tr>
<th>Authors (year)</th>
<th>Sample</th>
<th>Cannabis use measure</th>
<th>Outcome (measure)</th>
<th>Controls</th>
<th>Adjusted odds ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SYMPTOMS</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bovasso (2001)</td>
<td>1,920 American males and females from a population cohort</td>
<td>Cannabis abuse at baseline (DISa)</td>
<td>Any depressive symptom (ever) lasting 2 weeks or longer measured at follow-up 14–16 years later (DIS)</td>
<td>Baseline depressive symptoms, age, gender, ethnicity, antisocial symptoms, marital status, educational achievement, household income, stressful life events, physical and mental health, symptoms of psychiatric disorders and other substance use.</td>
<td>4.0 (1.2–13.0)</td>
</tr>
<tr>
<td>Fergusson et al. (2002)</td>
<td>1063 New Zealander males and females from Christchurch birth cohort</td>
<td>Cannabis use since previous assessment at age 15 (i), 18 (ii) and 21 (iii)</td>
<td>a) Presence or absence of suicidal thoughts since assessment at age 15, 16, 18 and 21 (self-report)</td>
<td>Unmeasured fixed effects, adverse life events, deviant peer affiliations, alcohol use, age of leaving school and age of leaving home.</td>
<td>a) (i) 7.3; (ii) 3.6; (iii) 1.8</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>b) Number of suicide attempts since assessment at age 15, 16, 18 and 21 (self-report)</td>
<td></td>
<td>b) (i) 13.1; (ii) 3.3; (iii) 0.8</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Note: 95% CI not reported</td>
<td></td>
</tr>
<tr>
<td>Windle and Wiesner (2004)</td>
<td>829 American young adults from an initial sample of 1216 adolescents</td>
<td>Cannabis use at four occasions from 15.5 years to 17.5 years of age—grouped as five “trajectories” (see p54)</td>
<td>CES-D scores at average age 23.5 years</td>
<td>Adolescent—family support, alcohol use, friends’ use of alcohol/drugs, educational attainment, stressful life events. Adult—family cohesion, current cannabis and alcohol use, friends’ use of illicit drugs, educational attainment.</td>
<td>No significant relationship of depression scores to cannabis use trajectories</td>
</tr>
<tr>
<td>Authors (year)</td>
<td>Sample</td>
<td>Cannabis use measure</td>
<td>Outcome (measure)</td>
<td>Controls</td>
<td>Adjusted odds ratio (95% CI)</td>
</tr>
<tr>
<td>---------------</td>
<td>--------</td>
<td>----------------------</td>
<td>-------------------</td>
<td>----------</td>
<td>-----------------------------</td>
</tr>
<tr>
<td>Hayatbakhsh et al. (2007)</td>
<td>3,239 Australian males and females from the Mater University Study of Pregnancy birth cohort</td>
<td>Cannabis use retrospectively assessed at age 21 (self-report) Cannabis use was measured for late onset and frequent use (a), early onset and frequent use (b), sole use (c), and use with other substances (d)</td>
<td>Symptoms of anxiety and depression from the past 6 months measured at 14 (YSRb) and 21 (YASRc).</td>
<td>Gender, mother’s age and education, maternal marital status and quality, family income, maternal substance use, adolescent mental health, adolescent smoking status and alcohol use.</td>
<td>a) 2.3 (1.5–3.6) b) 3.0 (1.8–5.2) c) 2.1 (1.1–4.0) d) 2.7 (1.8–4.1)</td>
</tr>
<tr>
<td>Fergusson and Horwood (1997)</td>
<td>935 New Zealander males and females from Christchurch birth cohort</td>
<td>Past year cannabis use at age 16 and cannabis use between age 16 and 18 (CIDI used for latter)</td>
<td>DSM-IV diagnosis of depressive disorder at age 18 years (CIDI)</td>
<td>Maternal age, SESe, gender, changes of parents, parental history of offending, childhood sexual abuse, conduct problems, childhood IQ, self-esteem, novelty seeking, mood or anxiety disorder, alcohol abuse, daily smoking, juvenile offending, parental attachment and defiant peer affiliations.</td>
<td>No significant effect</td>
</tr>
<tr>
<td>Fergusson et al. (2002)</td>
<td>1063 New Zealander males and females from Christchurch birth cohort</td>
<td>Cannabis use since previous assessment at age 15, 16, 18 and 21</td>
<td>DSM-III-R and DSM-IV diagnosis of depression since previous assessment at age 15, 16, 18 and 21 (CIDI)</td>
<td>Unmeasured fixed effects, adverse life events, deviant peer affiliations, alcohol use, age of leaving school and age of leaving home.</td>
<td>1.7 (weekly cannabis use at all ages) Note: 95% CI not reported</td>
</tr>
<tr>
<td>Authors (year)</td>
<td>Sample</td>
<td>Cannabis use measure</td>
<td>Outcome (measure)</td>
<td>Controls</td>
<td>Adjusted odds ratio (95% CI)</td>
</tr>
<tr>
<td>---------------</td>
<td>--------</td>
<td>----------------------</td>
<td>-------------------</td>
<td>----------</td>
<td>-----------------------------</td>
</tr>
</tbody>
</table>
| Brook et al. (2002) | 736 American males and females from a community sample aged 1–10 years at baseline | Frequency of cannabis use retrospectively assessed 22 years later via self-report of use a) 8, b) 11, and c) 17 years after baseline. | DSM-IV diagnosis of MDD assessed 22 years after baseline (CIDI) | Prior episodes of MDD or substance use disorder, demographic factors, SES, and childhood aggression. | a) 1.6 (1.1–2.2)  
   b) 1.4 (1.1–1.9)  
   c) No significant effect |
| Patton et al. (2002) | 1601 Victorian high school students aged 14–15 at baseline | Frequency of cannabis use in the past 6 months during adolescence | Mixed depression and anxiety (CIS-Rg) at age 20–21—not as severe as anxiety or depressive disorders, but clinical intervention still appropriate | Adolescent depression and anxiety, alcohol use, antisocial behaviour, parental separation and parental education. | 1.9 (1.1–3.3) for females  
   No significant effect for males |
| Arsenault et al. (2004) | 759 New Zealander males and females from Dunedin birth cohort | a) Use of cannabis by age 15, continued use at age 18  
   b) Use of cannabis by 18 (no use at 15) | DSM-IVh diagnosis of depression at age 26 (DIS) | Gender, SES and other drug use. | a) No significant effect  
   b) 1.59 (1.01–2.49) |
<p>| Wade and Pevalin (2005) | 4,834 United States school children | Used cannabis in past 30 days (mean age 15) | Depression one year later (CES-D) | Age, gender, delinquency, alcohol and other substance use, SES, area of residence, ethnicity, and family, school and peer attachment. | No significant effect |</p>
<table>
<thead>
<tr>
<th>Authors (year)</th>
<th>Sample</th>
<th>Cannabis use measure</th>
<th>Outcome (measure)</th>
<th>Controls</th>
<th>Adjusted odds ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Harder et al. (2006)</td>
<td>8,759 United States males and females from population sample, aged 29–37 in 1994</td>
<td>a) Self-reported past year cannabis use in 1994 b) Self-reported past year cannabis use in 1998</td>
<td>a) Depression in the past week in 1994 (CES-Di) b) Depression in the past week four years later 2002 (CES-D)</td>
<td>Age, race, gender, general health limitations, region of residence, criminal activity, alcohol use, cigarette use, excessive alcohol use, use of hard drugs, depression, educational achievement and SES.</td>
<td>No significant effect after adjustment for a) or b)</td>
</tr>
<tr>
<td>Georgiades and Boyle (2007)</td>
<td>1,282 Canadian males and females from a general population sample aged 12–16 years at baseline (1983) or at the first follow-up (1987)</td>
<td>a) Any cannabis use in the past 6 months at age 12–16 (T1) b) Any cannabis use in past year at age 26–34 (T2) c) Any cannabis use at T1 and T2</td>
<td>12 month prevalence of MDD at T2 (CIDI)</td>
<td>Family SES, single parent home, family functioning, gender, age, grade failure, medical condition, health status, externalising and internalising syndrome scales.</td>
<td>a) No significant effect b) 2.6 (1.7–4.0) c) 4.5 (2.0–9.7)</td>
</tr>
</tbody>
</table>

Abbreviations:
DIS = Diagnostic Interview Schedule
YSR = Youth Self-Report
YASR = Young Adult Self-Report version of the Child Behaviour Checklist
CIDI = Composite International Diagnostic Interview
SES = Socioeconomic Status
MDM = Major Depressive Disorder
CIS-R = Computerised Revised Clinical Interview Schedule
DSM-IV = Diagnostic and Statistical Manual of Mental Disorders, fourth ed.
CES-D = Centre for Epidemiological Studies—Depression questionnaire
From the results summarised in Table 6.1, the majority suggest that the duration, frequency and intensity of cannabis use all seem directly related to the emergence of depression. If cannabis use is actually causing cases of depression, this indicates both cumulative and dose/response effects. Before accepting this conclusion, two points should be considered. As most studies have used diagnoses of depression rather than reported symptoms, they avoid the problem of extrapolating from the latter to the former. The greater prevalence of depression compared with disorders such as schizophrenia facilitates this. Controlling for reverse causality has generally been accomplished by assessing symptoms of depression. However, it is noteworthy that the study assessing changes in cannabis use more comprehensively [220] found that only increasing use was associated with current, but not later, depression scores.

Cognitive styles have been implicated in the development of depression for some time [221] [222], and have led to much better understanding of these disorders [223]. The ways in which the individual thinks about his or her own characteristics, interpersonal relationships and external events and the ways in which he or she copes with the less desirable aspects of these are strongly associated with the emergence of clinical depression. It is recognised that cognitive style [221] and coping style [224] are both part of the depressive syndrome and often precede the emergence of clinical depression by some time [207]. In particular, the avoidant coping style that predicts poorer prognosis in depression [225] also predicts drug use [226] and poorer drug treatment outcomes [227]. An alternative explanation for the results in Table 6.1 is that maladaptive cognitive and coping styles precede both drug use and depression.

Many of the cannabis-depression studies report any cannabis use, some threshold use, or arbitrary levels of light/heavy use rather than quantity or frequency, obscuring any dose-response relationship. Confounding factors were controlled for comprehensively in some studies (e.g. the Christchurch studies), but not in others (e.g. the studies that assessed adult populations and could therefore not control for early childhood and family factors).

Thus it is unclear whether cannabis causes depression that would not have otherwise occurred, or whether it is triggering it in vulnerable individuals who would have experienced depression anyway. Despite these limitations, the studies shed more light on the relationship between cannabis and depression than had previously been available [205]. Frequent and continued use of cannabis is associated with increased risk of experiencing depressive symptoms or depressive disorder in adulthood.

### 6.2 Reverse causality: Do mood disorders lead to cannabis use?

Most studies that did assess reverse causality, or the self-medication hypothesis found no evidence to support this [228][214][216][217][229][82]. However, a very recent study has found an association between MDD and later cannabis use and cannabis use disorder [230], and as mentioned earlier, the LAT study found a similar relationship [220]. While these studies do not directly support the cognitive/coping style model, they are consistent with it. While there is better evidence that those with developing mood disorders may use cannabis to manage their symptoms, this seems more important for, and may be limited to, females. However, assuming that depressive symptoms are the best long term predictors of major depression may not be an appropriate way to test this model.
The reported effects of cannabis, particularly temporary euphoria and relief of anxiety, support its use for symptomatic relief. A more speculative suggestion is that the sense of enhanced understanding reported by many cannabis users may counteract the feeling of meaningless that often accompanies depression.

The most salient factor in the relationship of mood disorders and cannabis is the association of childhood and adolescent conduct disorders with both bipolar disorder and drug use. Maladaptive coping styles, particularly avoidant or escapist, may facilitate the use of recreational drugs to deal with emerging mood and anxiety disorders.

6.3 How does cannabis compare to other risk factors for depression?

In common with other psychiatric disorders, vulnerability to depression is heritable. A meta-analysis of studies estimated the heritability of major depression at 37% [231], and a more recent twin study, the aggregate estimate was 38% [193]. Interestingly, the latter study found that the estimated heritability in women (42%) was significantly higher than in men (29%), a result also noted in an Australian twin study [232]. The effect of heritability is clearly stronger than that of infrequent cannabis use, with only frequent, long-term users approaching the liability of those with a parent who has experienced MDD.

Apart from the stronger heritability, females are at risk of depression from a higher probability of being sexually abused [233], pregnancy and childbirth [234], miscarriage [235], menopause [236] and a variety of other gender-biased influences [233]. The approximate doubling of the lifetime risk of depression in women is at least in part due to the aggregation of such factors.

Polydrug abuse, in particular with combinations like alcohol and cocaine [237], is a strong risk factor for depression. It is notable that polydrug use may be a better predictor of depression than any single drug [238][239], even with therapeutic drugs [240]. This may underlie the disappearance of some drug effects when controlling for other drug use [236]. Reports of polydrug use commencing after the onset of depression [241] suggest a bidirectional association.

Physical impairment, whether acute or chronic, is commonly accompanied by depression [242]. Overall, the more severe or life-threatening the impairment, the greater the risk of depression.

6.4 What is the mechanism of the relationship?

The widely acknowledged association of maladaptive coping styles with emerging depression provides one plausible mechanism for its association with cannabis use. First, as there is little evidence that cannabis directly exacerbates the symptoms of depression, its use as a temporary euphoriant or mood stabiliser is plausible. An avoidant style of coping includes the tendency to use drugs to deal with stressors rather than recruit effective responses. The similar use of tobacco is consistent with this interpretation [243]. A causal model would predict that subclinical depression is ineffectively managed with cannabis, thus delaying treatment.
Alternatively, cannabis use may gradually enhance the underlying causes of depression, either directly by altering neurochemical activity [244] or affecting cognitive factors such as perceptions of rejection, inferiority or abnormality that arise from the interpersonal and social consequences of cannabis use. Current theories of the aetiology of depression emphasise cognitive style as a crucial part of vulnerability to depression [222][223], and suggest that cognitive style, rather than depressive symptoms, is a better predictor of emerging depression.