Background
Cannabis is the most widely used illicit drug in Australia. Regular use has been associated with increased risk for a range of harms, including the development and exacerbation of mental disorders.

Objective
This article reviews current evidence relating to the neuropharmacology of cannabis and its impact on mental health, as well as strategies related to the assessment and management of cannabis and co-occurring mental disorders within the primary care setting.

Discussion
Early and heavy use of cannabis has been associated with the onset of psychosis and depression, while chronic use results in poorer treatment outcomes among those with co-occurring mental disorders. Effective management involves the development of therapeutic engagement and an ongoing relationship, with monitoring of cannabis use and mental health problems. Standard pharmacotherapeutic treatment of the mental disorder may be associated with a reduction in cannabis use, although adjunctive psychological intervention is also likely to be required.

Keywords: mental health; substance related disorders; general practice; cannabis

Cannabis, derived from the plant Cannabis sativa, is the most widely used illicit drug in Australia. Approximately one-third of the population have reported cannabis use at some time in their life, with around 9% reporting use in the past 12 months. Over the past few decades, the proportion of young people who have used cannabis has steadily increased while the age of first use has declined. An earlier onset of use increases the risk for subsequent dependence, while regular use during adolescence predicts later use of other illicit drugs, underperformance in school and mental health problems.

Cannabinoids
There are more than 60 different cannabinoids found within Cannabis sativa, although they vary considerably in the extent to which they are psychoactive. The two most abundant naturally occurring cannabinoids are Δ9-tetrahydrocannabinol (THC) and cannabidiol (CBD), but these have markedly different (and almost opposing) effects. While THC is psychotomimetic and accounts for the 'high' associated with cannabis use, CBD has been found to be anxiolytic and to have antipsychotic properties. Variations in the ratio of these two cannabinoids in illicit cannabis supplies is therefore likely to impact on the intensity and quality of the associated experience. Indeed, a recent study examining levels of THC and CBD in hair samples of cannabis users and nonusers found that users with THC alone reported higher levels of positive schizophrenia-like symptoms, while the THC and CBD group reported less anhedonia.

Neuropharmacology
Δ9-tetrahydrocannabinol is highly lipid soluble, allowing it to pass readily across the blood-brain barrier. Its psychoactive properties relate to the activation of an endogenous cannabinoid system that is densely distributed throughout the brain. Two types of cannabinoid receptor (CB1 and CB2) have been discovered to date. The CB1 receptor, which is present in high densities on axons and nerve terminals of the cerebral cortex (especially frontal regions), hippocampus, basal ganglia and cerebellum, is thought to mediate the intoxicant effects of THC, especially as CB2 receptors are found...
mainly on cells of the immune system. Activation of CB1 receptors, which are predominantly presynaptic, modulate the release of other neurotransmitters (eg. gamma-aminobutyric acid [GABA], glutamate, serotonin) in these brain regions. Just like other drugs of abuse, THC is reinforcing because of its ability to release dopamine within the brain’s reward system, although the mechanism is indirect, ie. by switching off GABA interneurons that normally tonically inhibit these dopaminergic pathways.

**Impact on mental health**

The acute psychoactive effects of cannabis include a sense of calmness and relaxation, euphoria and perceptual alterations, including time distortion and the intensification of emotions or experiences. However in some individuals, unpleasant reactions to cannabis may occur. These include depression, paranoia, anxiety or panic attacks. In fact, high dose intravenous THC given acutely produces transient symptoms and deficits (ie. positive and negative symptoms, perceptual alterations, anxiety, deficits in working memory, recall, and the executive control of attention) that closely resemble those observed in people with chronic psychotic disorders, implicating the endocannabinoid system in the pathophysiology of schizophrenia. Consistent with this notion, reductions in brain regions (ie. hippocampus and amygdala) associated with psychosis and depression have been reported in long term heavy cannabis users, together with related cognitive deficits.

**Cannabis and psychosis**

The hypothesis that cannabis is a risk factor for psychosis has received support from a number of recent longitudinal cohort and population based studies. Regular cannabis use appears to be associated with an approximate twofold increase in the relative risk of developing schizophrenia or other psychosis outcomes, with greater risk among those who use cannabis more frequently. However, while cannabis (particularly adolescent onset and heavy use) is a risk factor for later psychosis, the incidence of schizophrenia does not appear to be increasing despite elevated rates of cannabis use in the general community. This suggests that the relationship between cannabis use and psychosis is particularly complex, and highlights the need for prospective studies that examine how cannabis use during adolescence affects a range of developmental processes (including brain maturation). Nevertheless, among people with psychosis, chronic cannabis use impacts negatively on both illness course and treatment outcome, and is associated with poor medication compliance, more severe psychotic symptoms, and earlier and more frequent psychotic relapses.

**Cannabis and affective disorders**

Patton and colleagues found that early onset weekly cannabis use in adolescence predicts a twofold increase in rates of depression among young women, with daily use increasing the risk fourfold. Several other epidemiological studies have also reported higher levels of depression among cannabis users, although a recent systematic review highlighted that the association is modest and noncausal explanations often remain unaddressed within studies. Nevertheless, using drugs (mainly cannabis) to cope with negative affect is commonly reported by young people presenting to mental health services for mood or anxiety disorders, highlighting the importance of targeting coping skills during treatment. Indeed, young people with co-occurring affective and substance use disorders continue to experience substantial problems with symptoms and functioning 6 months after presentation to mental health services, suggesting that integrated approaches that address both the mental health and cannabis use simultaneously should be considered.

**Screening and assessment**

Identification of cannabis use and accompanying mental health problems is best undertaken with a nonjudgemental and empathic approach that allows for the development of therapeutec engagement and an ongoing relationship. It is important to familiarise yourself with possible signs of cannabis dependence and associated psychiatric features. Relevant clinical features include:

- statements from the patient or observations by others about cannabis being used to assist with emotional regulation
- reports of low mood or mood swings
- loss of enjoyment in activities
- lowered functioning, or
- a significant shift in weight

Relevant sociodemographic factors include:

- a family history of substance misuse
- homelessness
- disruptive behaviour
- poor family relationships
- repeated hospitalisations, and
- legal difficulties

Lampropoulos’ recommendations regarding the assessment process for identification of drug abuse and associated problems are helpful:

- allow the person to attend either individually or with a support person, depending on their preference
- assure confidentiality and explain its limits
- use a framework such as HEADSS (Home, Education and employment, Activities, Drugs, Sexuality, Suicide and depression). The HEADSS approach is particularly helpful as it starts with the least threatening areas, allowing rapport to develop, and places substance use in context as well as helping to identify comorbid issues.

To enhance open communication, begin with general questions about use of legal substances such as alcohol and tobacco, and of prescribed medications, thus opening up the subject area of cannabis use in a nonthreatening manner. Likewise, start with general questions about mental health, asking about worries or concerns (rather than ‘anxiety’) and periods of feeling low or down (as opposed to ‘depression’) before moving to ask about any other symptoms which emerge during the interview. Use of a screening tool can be helpful in eliciting a history of cannabis use and associated mental health problems, and the following are particularly suitable within the primary care setting:
• The Psychosis Screener\textsuperscript{22} (six questions about lifetime psychotic symptoms)
• The Kessler Psychological Distress Scale\textsuperscript{23} (K10: 10 items measuring psychological distress indicating the likelihood of anxiety and/or depression)
• The PsyCheck Screening Tool\textsuperscript{24} (three components: general mental health history and treatment, a formal, structured suicide risk assessment, and a modified version of the World Health Organization developed self reporting questionnaire (SRQ)\textsuperscript{25} which assesses current symptoms of depression, anxiety and somatic complaints). The PsyCheck asks the person whether each mental health symptom has ever occurred during a period of abstinence
• The Alcohol, Smoking and Substance Involvement Screening Test\textsuperscript{26} (ASSIST: an eight item interviewer administered screen for all types of substance use, accompanied by guidelines for brief intervention). As many cannabis users are polydrug users, the ASSIST is informative as it gives a quick and broad picture of overall substance use involvement
• The Severity of Dependence Scale\textsuperscript{27} (SDS: five items, employed when problematic use has been identified)
• The Cannabis Use Disorder Identification Test revised\textsuperscript{28} (screens for problematic cannabis use and consists of eight items, two each from the domains of consumption, cannabis problems [abuse], dependence, and psychological features).

Management

As discussed, many young people may be using cannabis to cope with negative affect, and affective or psychotic disorders frequently co-occur with substance use disorders. Therefore, integrated approaches that address both the mental health and cannabis use are required.\textsuperscript{15,16} A summary of management strategies is outlined in Table 1.

As with assessment, a nonjudgmental and empathic approach to management is likely to lead to better outcomes. In addition, using motivational interviewing techniques\textsuperscript{29} enhances the likelihood of change.

Allow the person to identify their own goals and facilitate this by identifying their stage of change using a ‘readiness ruler’.\textsuperscript{29} On a scale from 1 to 10, how important is it for you to reduce your cannabis use?

If the person gives a low number, engage the person in a motivational interviewing decisional balance exercise, ‘What are the good things about cannabis use? And what are the less good things about cannabis use?’ It may also be helpful to ask, ‘What would it take to move you up to an 8 for importance?’

Link cannabis use to the presenting mental health symptoms by asking, for example, ‘How does the cannabis use affect your mood/worrying?’ Provide information on the possible relationship with the person’s presenting symptomatology (referring back to any information from screening instruments) and seek their feedback, ‘How does that sound to you?’

If the person rated importance highly, move on to assess confidence\textsuperscript{29} by asking, ‘How confident are you that you can reduce your cannabis use?’ If confidence is high, ask what ideas they have about how to go about change. If a low number is given, seek permission to give information about possible helpful strategies, ‘I wonder if you would be interested to hear what others have found helpful in this situation?’ Negotiate a change plan for cannabis use and associated mental health problems, by asking something like, ‘So, what’s the next step?’

If the person is not ready to quit cannabis use, work with them on a harm minimisation goal, keeping the door open to potential quit attempts in the future.

At present there is no evidence based pharmacological intervention for managing cannabis withdrawal. However, there is evidence that effectively treating the mental disorder (psychosis or depression) with standard pharmacotherapy may be associated with a reduction in cannabis use, although adjunctive psychological treatment is also likely to be required.\textsuperscript{31} Cannabis use declines (at least in the short term) with psychological treatment, including psychoeducation, self help booklets, brief motivational interviewing interventions and cognitive behaviour therapy (CBT). Computer delivered CBT for co-existing depression and cannabis use has been shown to be effective.\textsuperscript{32} In people with psychosis, CBT has been associated with improvements in general functioning at longer term follow up and it is possible that more distal improvements in cannabis and other drug use occur as functioning improves.\textsuperscript{33,34} Relapse appears to be common among heavy cannabis users, suggesting that ongoing monitoring and intervention within the primary care setting may be helpful. Taking a longer term perspective and encouraging healthy lifestyle, vocational and social activities, particularly in people with psychosis, is likely to be helpful.\textsuperscript{35}

Resources

• National Cannabis Prevention and Information Centre provides information for those experiencing problems with cannabis use, free resources and training on related issues and a national helpline: 1800 30 40 50; www.ncpic.org.au

Table 1. Management of cannabis use/dependence and associated mental health problems

| 1. Screen for cannabis use and associated mental health problems |
| 2. Identify stage of change regarding cannabis use with readiness ruler |
| 3. Use decisional balance (good things/less good things about cannabis use) |
| 4. Ask about possible link between cannabis use and presenting mental health symptoms |
| 5. Seek permission to provide information |
| 6. Assess confidence to reduce cannabis use with confidence ruler |
| 7. Explore options for change |
| 8. Negotiate a change plan: ‘What’s the next step?’ |
| 9. Optimise pharmacological treatment of mental disorder and/or referral for psychological intervention |
| 10. Regularly monitor cannabis use and mental health symptoms over time to prevent or address relapse |
• Mental Health First Aid provides guidelines on how to help a person developing a mental health or substance use problem. There is a guideline for cannabis use: www.mhfa.com.au
• SANE Australia is a national charity working for a better life for people affected by mental illness. It provides information and fact sheets on mental health problems and substance use, including cannabis: www.sane.org.au.

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References