Cannabis and human behaviour: Harmless relaxant or evil weed?

By Edward Ogden

Cannabis is the most prevalent illicit drug in use in Australia: 39% of Australians over 14 have tried it. One in five men and one in six women has used cannabis in the last 12 months,[1] while one in 10 men and one in 20 women reports using cannabis in the past month.[2] Contrary to earlier beliefs, recent motor vehicle accident data suggest that the use of cannabis is associated with elevated culpability in crashes.

Those who favour legalising cannabis point out that it has been used as a medicine to treat a wide range of conditions including nausea and vomiting, epilepsy, paraplegia, AIDS, chronic pain, migraine, chronic itch, labour pain, menstrual cramp, weight loss, insomnia, lymphoma, glaucoma, multiple sclerosis, depression, and other mood disorders. The argument for continuing controls relies on the evidence that it is just as likely to cause cancer as other smoked vegetation and in addition suppresses the immune system, stimulates the circulation, and impairs fertility. Cannabis use in adolescence is associated with poor educational performance and other undesirable social outcomes. There is reasonable evidence that heavy cannabis use can produce an acute psychosis and may induce a schizophrenic illness in susceptible individuals.[3]

The acute effects of cannabis depend on the dose, the mode of administration, the user's prior experience with the drug, concurrent use of other drugs and the user's expectations. This is further complicated by the reality that it is a natural plant extract that varies in potency by a factor of 10 or more. Most users experience a 'high' characterised by mild euphoria and relaxation, time distortion, and intensification of ordinary sensory experiences. At the same time, many forms of skilled psychomotor activity are impaired. The most common acute adverse effects of cannabis are anxiety, unpleasant mood change, panic and paranoia, particularly among naive users. There is some evidence to suggest that, after alcohol, >>

cannabis accounts for more drug use disorders than any other substance.[1,4,5]

WHAT IS CANNABIS?

Cannabis (marijuana) is a mixture of the dried flowering tops and leaves of the plant *Cannabis sativa*. Like most natural materials derived from plants, it is a variable and complex mixture of many chemical compounds, some of which are pharmacologically active. Marijuana contains more than 400 chemicals. Approximately 60 are called 'cannabinoids' and are found in no other plant. The most active of these compounds is delta-9-tetrahydrocannabinol, which is abbreviated to $\triangle^9$-THC or more simply THC. Varying proportions of other cannabinoids, mainly cannabidiol (CBD) and cannabinol (CBN), are also present, sometimes in significant quantities that cause effects of their own. CBD is not psychoactive but has significant other pharmacological activity.

The concentration of cannabinoids in marijuana varies greatly depending on growing conditions, plant genetics, and processing after harvest. In the usual mixture of leaves and stems distributed as marijuana, concentration of THC ranges from 0.3% to 4% by weight.

However, specially grown and selected marijuana can contain 15% or more THC. Thus, a marijuana cigarette might contain anywhere from 3 mg to 150 mg or more THC.

Cannabis has been variously classified as a narcotic, a sedative and as an hallucinogen, but it is actually in a class of its own. It acts on specific receptors in the brain that are found in the parts of the brain associated with cognitive functions. A naturally occurring brain hormone (anandamide) also binds to these receptors and is thought to have a role in the sensation of pleasure. This may explain some of the drug's appeal.

THC is quite potent. An intravenous dose of 1 mg can produce profound effects. However, despite being quite a potent drug with effects on several organ systems, lethal doses in humans are not known.

Marijuana is typically smoked like tobacco or mixed with tobacco either as a cigarette ('a joint') or in a water pipe ('a bong'). Marijuana extracts can also be incorporated into foods or alcoholic beverages. Pure preparations of cannabinoids can be administered by mouth, by rectal suppository, by injection, or smoked.

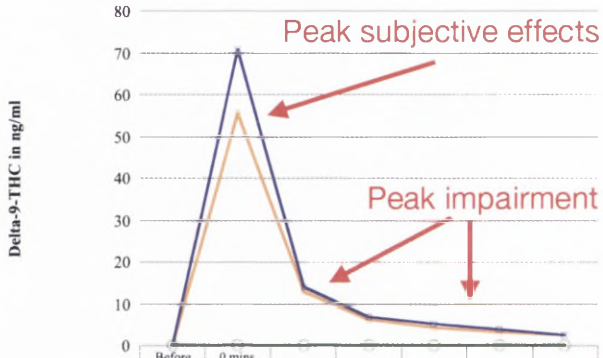
When marijuana is smoked, 10% to 50% of the THC and other cannabinoids present enter the circulation within seconds and are rapidly delivered via the bloodstream to the brain.[6] Peak blood levels appear about the time smoking is finished, whereas THC or marijuana consumed by mouth takes several hours to reach a peak and the effects are delayed.

On entering the bloodstream, cannabinoids are distributed rapidly throughout the body. Cannabinoids are highly fat soluble, and accumulate in fatty tissues from which they are very slowly released back into the blood stream. The half-life of THC is approximately 56 hours in occasional users and 28 hours in chronic users. However, the tissue half-life is approximately seven days and complete elimination of a single dose may take up to 30 days. THC is mostly metabolised to an inactive metabolite, 11-nor-9-carboxy-delta-tetrahydocannabinol (THC-COOH), although at least 80 other metabolites are also formed.

The tissue half-life of THC is estimated to be as long as 10 days and various metabolic products can be found for several weeks after exposure.

Impairment and THC levels

THC Levels after smoking placebo, low and high dose cannabis cigarettes



	Before Smoking THC	0 mins after smoking	20 mins	50 mins	75 mins	100 mins	125 mins
Placebo	0	0	0	0	0	0	0
1.74% THC	0	55.46	12.84	6.16	4.32	3.18	2.53
2.93% THC	0	70.59	13.85	6.79	5.13	3.72	2.42

Recent motor vehicle accident data suggest that the use of cannabis is associated with elevated culpability in crashes.

BLOOD, SWEAT AND TEARS

Most body fluids have been examined for forensic purposes.

Blood

As noted above, the cannabinoids are insoluble in water, but very soluble in fat. THC levels in blood are only indirectly related to levels in the brain and not a direct measure of intoxication.

THC levels in blood are highest as smoking ceases and fall within minutes. An hour later they are about 5% to 10% of the peak level at the time when there is the greatest effect on performance.

Cannabinoids are slowly released from tissues and slowly eliminated from the body. Plasma levels of THC >5µg/L are suggestive of recent consumption and presumptive evidence of intoxication. If the levels of THC and THC-COOH are similar, then marijuana was probably used within the previous 20-40 minutes and intoxication is likely. If THC-COOH levels are greater than THC, use was probably more than 30 minutes ago (in a naive user). Values of THC-COOH in blood greater than 40µg/L indicate chronic consumption.

Sweat

Cannabis metabolites are deposited on the skin with perspiration and skin swabs can be used to detect the presence of the drug. Detection threshold is reported to be about 10µg/L THC.

Urine

Urine tests are non-invasive and useful for screening. High levels of cannabinoids in the urine, particularly the water soluble THC-COOH, appear within 30 minutes of consumption and are present for days after exposure. Frequent or habitual consumers may excrete metabolites for weeks as they clear cannabinoids from fatty tissues.

Saliva

Saliva sampling can be used to establish recent consumption and is relatively easy and non-invasive. Concentrations of more than 5µg/L THC are indicative of recent consumption and appear to correlate with subjective intoxication and heart rate.

MEDICAL USE OF CANNABIS

Claims have been made that cannabis is beneficial in the treatment of neuralgia, gout, tetanus, hydrophobia, cholera, convulsions, chorea, hysteria, depression and insanity. In Australia, tincture of cannabis was used in medicines until the 1960s, when it was declared a prohibited drug.[8]

Since recreational use of cannabis has been prohibited, its use for medicinal purposes has been unpopular, although the therapeutic benefits of cannabis have received close attention at various times. In 1991, an anonymous survey of members of the American Society of Clinical Oncology measured the attitudes and experiences of cancer specialists with using cannabis to treat nausea in chemotherapy patients. Of the 43% of recipients who responded to the survey, more than 44% of them had recommended the illegal use of cannabis for at least one cancer patient. Almost half said that they would prescribe cannabis to some of their patients if it were legal.[9, 10]

Cannabis has been used as an anti-emetic in the treatment of AIDS patients and as a painkiller for those suffering from chronic pain. It has also been effective in reducing intra-ocular pressure in glaucoma patients and in treating epilepsy, Huntington's chorea and Parkinsonian tremor. Its place in medical treatment in Australia remains controversial.[1, 3, 11]

RECREATIONAL USE OF CANNABIS

The major motivation for recreational use of cannabis is the experience of a subjective 'high' which is characterised by mild euphoria and relaxation, distortion of time, and intensification of ordinary experiences. The 'high' is often >>

accompanied by infectious laughter, talkativeness and increased sociability. The user often becomes lost in daydreams and has difficulty completing mental tasks. While some students report that cannabis makes study easier, there are cognitive changes including memory loss that mean it is inefficient. Motor skills, reaction time and motor co-ordination are affected, which means that skilled psychomotor activity is affected.

Not all of the experiences during cannabis use are pleasant. Users also report panic reactions, depressed mood and fear of 'going mad'.

There is no defined toxic level for cannabis. There is no case of death attributable to cannabis in the world medical literature. Extrapolation from the animal evidence suggests the toxic dose of THC in an adult would be about 9kg!

LIMITATIONS OF MARIJUANA RESEARCH

Much of what is known about the pharmacology of marijuana comes from experiments with purified THC. The pharmacology of THC alone may not be the same as the pharmacology of smoked marijuana containing the same amount of THC. The alternative models have used plant material containing up to 4% THC smoked by relatively young, medically screened, healthy volunteers experienced with the effects of marijuana. This group may not be typical of the 'real world' population of marijuana users.

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EFFECTS OF MARIJUANA ON THE BRAIN

The commonly reported mental and behavioural effects of marijuana consist of a sense of well-being, relaxation, altered perception of time and distance, and intensified sensory experiences. Acute consumption is associated with impaired memory for recent events, difficulty concentrating, dreamlike states, impaired motor co-ordination, impaired driving and other psychomotor skills, slowed reaction time, impaired goal-directed mental activity, and altered peripheral vision.

Tolerance rapidly develops to many of the subjective and physiological effects with repeated use, so that the perceived intensity of the effects of a given dose is modified by past experience.

After a single dose of THC, most mental and behavioural effects are measurable for only a few hours and are no longer measurable after four to six hours.

ADVERSE MENTAL EFFECTS

Large doses of marijuana can produce transient anxiety, panic and feelings of depression, depersonalisation, bizarre behaviour, delusions and hallucinations. Some individuals appear especially sensitive to marijuana and will experience severe reactions to relatively small doses.

The unpleasant effects are usually of sudden onset, during or shortly after smoking, and last a few hours. They do not require specific treatment other than reassurance in a supportive environment. A psychotic state with features like schizophrenia or mania has been described. Chronic marijuana use is often associated with apathy and loss of motivation, along with impaired educational performance.

MARIJUANA AND DRIVING

Laboratory studies

The first reported study using a driving simulator concluded that marijuana (22mg THC) increased the number of errors in monitoring the vehicle's speedometer.[12] Almost 20 years ago, Moskowitz summarised the research as showing that low doses of marijuana showed no effects on car control, other than slowness of decision-making and impairment of perception.[13]

Recent studies using more realistic simulations of driving and examining a wider range of variables tell a different story. For instance, smoking low-dose THC cigarettes showed

changes in braking similar to driving with a blood alcohol concentration of .05%.[14] Local research has also demonstrated that the consumption of low and high doses of cannabis is associated with an increase in lane-weaving.[15]

On-road studies examining the effects of cannabis on driving performance have been conducted over the past decade. Participants on a closed driving circuit set out with cones and poles were instructed to drive as quickly as possible. Results showed that marijuana consumption resulted in poor car-handling, with the number of cones hit related to the dose of THC.[16] More recently, a team at Maastricht University examined on-road driving with various low doses of THC, and found that THC impaired driving.[17] High doses of THC have never been systematically studied, but can be predicted to produce even larger impairment. Detrimental effects of THC were more prominent in certain driving tasks than others. Highly automated behaviours, such as road-tracking control, were more affected by THC than more complex driving tasks requiring conscious control.[18]

Epidemiology

The risk of driving after consuming alcohol has been demonstrated in several large epidemiological studies in which breath alcohol levels in crash-involved drivers were compared with control drivers who had not crashed. The probability of involvement in a collision was determined for each blood alcohol concentration by comparing the relative number of collision-involved drivers at each blood alcohol concentration in the crash group with the relative number of non-collision-involved drivers at the same blood alcohol concentration in the control group.[19-21] There is no comparable study for THC.

Part of the problem is that THC has been difficult to measure until quite recently. Many of the older assays did not distinguish active THC from the inactive metabolite. In a series of studies, Drummer and colleagues have collected toxicology data for drivers killed in vehicle crashes and determined their culpability for the collision according to a set of rules. Drivers were classified as culpable, contributory, or not culpable. The mitigating factors used in the analyses were the condition of the road and vehicle, driving conditions, type of accident, witness observations, road law obedience, difficulty of the task involved, and the level of fatigue.[22] The relative ratio of 'culpable' to 'not culpable' for the presence or absence of drug gives an indication of the risks of the substance being present. The original work showed a low relative-risk for cannabis that might even have been interpreted to mean that cannabis use reduced the risk of fatal collision!

A more recent analysis of 3,398 fatally injured drivers across Victoria, NSW, and Western Australia between 1990 and 1999 came to quite different conclusions. Improved analytical techniques, which determine the level of THC rather than the inactive metabolite, found active THC in just over half the samples in which cannabinoids were detected. THC was associated with increased culpability for both car drivers (relative risk 2.7 times) and motorcyclists (relative risk 2.4 times). The majority (84%) had THC levels > 5 µg/L and, at this level, the risk of being responsible for the collision was 6.6 times higher than for those drivers found to be drug-free. This is similar to the risk of driving with a blood alcohol concentration greater than 0.15%.

The only possible conclusion is that a THC level greater than 5 µg/L is grossly impairing of driving skill and is evidence of recent use of marijuana.

ATTITUDES TO DRIVING WITH CANNABIS

In 2002, Australian Associated Motor Insurers Ltd (AAMI) published its second annual Young Driver Index, which was based on the company's insurance claims, and an independent survey of 1,184 licensed drivers of all ages living in the eastern states and capital territory of Australia.

Overall, 15% of drivers aged 18-24 reported driving after using recreational drugs. Of young drivers, 8% (higher among males) and 5% of older drivers thought that using a small amount of recreational drugs before driving did not affect their driving ability. Young drivers were more likely than older drivers to consider that driving after using recreational drugs was safer than driving after drinking (15% versus 7%).

A Queensland study of university students examined the incidence of drugged driving and attitudes towards drugged driving: 26% of the sample surveyed admitted to driving while under the influence of drugs. The strongest predictor of the incidence of drugged driving was drug use: if subjects >>

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admitted to drug use they were likely to drive under the influence. The factors that influenced their attitudes were the opinions of their peers and lack of perceived harm. Their attitude to drink-driving was based more on risk of detection and peer norms.[23]

Behavioural testing

In the US, concerns about civil liberties impeded the development of random breath-testing programs. The US Department of Transportation commissioned work during the late 1970s to develop a standardised field sobriety test battery that would facilitate the accurate recognition of intoxicated drivers in the field. The result was a battery of observations that became known as the Standardised Field Sobriety Test (SFST).

The SFST battery was demonstrated to be a reliable screening tool for alcohol in a Finnish study involving more than 5,000 subjects.[24] Some 20 years after developing the SFST, Burns posed the question: 'How accurate are trained and experienced officers when they base roadside decisions on the SFST?' She conducted a study of arrest decisions in Colorado that concluded that '94% of arrest decisions were correct' at a blood alcohol concentration of 0.05% and 97.5% of decisions were correct at a blood alcohol concentration of 0.10%.[25]

THC levels in body fluids have such poor correlation with behaviour that demonstration of impairment requires performance-testing rather than biochemistry. The SFST battery has been adopted in Victoria as the basis of drug prosecution.[26] The use of SFST as a 'pass/fail' test for marijuana was examined by the Drugs and Driving Unit at Swinburne University.[7, 27, 28] There was a significant relationship between THC level and the probability that SFST will classify an individual as impaired.[29]

IS THERE A FORENSIC FUTURE FOR THC?

Law enforcement is turning its attention not just to THC and driving, but also to the problems of THC in the workplace.

Victoria has begun a trial of random drug-testing of drivers using saliva as a screening test.[30] NSW is planning a trial this year.[31] Most developed nations have legislation prohibiting drugs and driving and the International Council on Alcohol, Drugs and Traffic Safety has recommended roadside screening and compulsory testing of drivers, especially those in the transport industry.[32]

The Standing Committee on Family and Community Affairs of the Australian Parliament concluded that there is not enough known about the role of drug impairment in the workplace. The Committee noted that what little data we have is over ten years old and inconsistently collected across the jurisdictions.[33] The 2001 National Drug Strategy (NDS) Household Survey reported that 4.3% of respondents reported having gone to work during the past 12 months when affected by alcohol, and 2.3 per cent went to work under the influence of other drugs.[2]

The availability of screening tests and reliable assays for THC means that there will be a great deal more reliable research data in the next few years. Legal practitioners will need to stay abreast of the new body of knowledge that links recreational drug use to impairment and the adverse outcomes of impaired performance. ■

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