CANNABIS AND ECSTASY – SOFT DRUGS?

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CANNABIS

After tobacco and alcohol, cannabis is one of the most widely used of all "recreational" drugs. In Britain and the USA nearly half of all 18 year olds admit to having tried the drug and 10-20% of 16-24 year olds are current users. Because the active ingredient in herbal cannabis, delta-9-tetrahydrocannabinol (THC), is poorly absorbed when taken orally and is too insoluble to inject, the drug is most commonly administered by smoking. THC acts on specific receptors on the surface of some brain cells; these receptors are normally activated by anandamide and related chemicals made naturally in the brain as part of a chemical signaling system.

THC has complex effects on brain function. It affects movement and balance control, distorts the sense of time, reduces sensitivity to pain and increases appetite. Users take the drug for the pleasant feelings of relaxation, social ease and the state of heightened perception and euphoria which accompany the cannabis "high".

There is a large literature on the effects of cannabis in human subjects (reviewed by Hollister, 1986, 1998; Iversen, 2000, 2002). The acute effects of the drug are relatively benign. There are virtually no cases of death from overdose, and cannabis intoxication is usually not accompanied by the increased aggression and violence often associated with alcohol. As with other intoxicants, driving under the influence of cannabis is not recommended – although the impairments measured in driving-simulators are relatively modest.

The chronic use of cannabis, however, carries some more serious hazards – although these tend to have been exaggerated in the official messages currently conveyed to young people. Possibly the most serious risk is related to the fact that the drug is commonly administered by smoking – often in the UK in combination with tobacco. Cannabis smoke contains many of the same noxious chemicals present in tobacco smoke, and it causes lung irritation which can lead to bronchitis. There is as yet no evidence for an increased risk of lung cancer in cannabis users, although some small-scale clinical studies have suggested an increased risk of cancers of the mouth and throat. Regular cannabis users may become dependent on the drug, and they may seek treatment to break their habit. It has been estimated that approximately 10% of those who use cannabis become dependent. On the other hand, the majority of cannabis users quit before the age of 30.

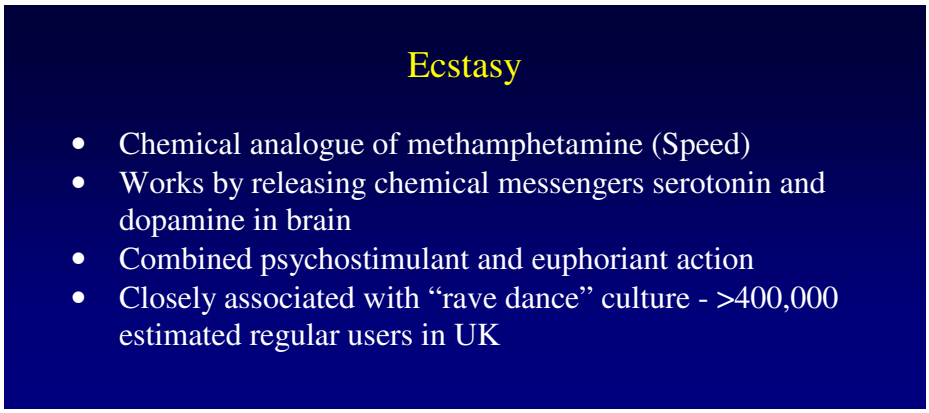
Earlier alarms about the alleged ill-effects of cannabis on reproductive function, the immune system and the so-called "amotivational state" have proved unfounded, as have claims that the drug can cause permanent brain damage. Controversy remains about the relationship between cannabis use and psychiatric illness. Whilst cannabis tends to exacerbate the symptoms of those already suffering

such illnesses, the evidence that cannabis may actually provoke long-term psychiatric breakdown is far less clear (Iversen, 2002).

ECSTASY (3,4-METHYLENEDIOXY-METHAMPHETAMINE)

This amphetamine derivative became widely used on both sides of the Atlantic during the 1980s and 1990s as an integral part of the "rave dance" culture. In Britain 9% of 16-29 year-olds have used ecstasy and among participants in the dance scene 80% admit using the drug (Milroy,1999). Ecstasy works on the brain by interacting with nerve cells that utilize the chemical messengers dopamine, noradrenaline and serotonin to promote increased release of all of these chemicals. The result is a combination of the psychostimulant actions of amphetamine (which acts mainly by increasing dopamine release) and the mild mind-altering properties of mescaline (which acts mainly on the serotonin system). Ecstasy users report feeling happy, relaxed and warm towards others. The amphetamine-like actions help users to stay awake for all-night dance sessions.

Unlike cannabis, the acute use of ecstasy has been associated with deaths, with 27 recorded in the year 2000 (Milroy, 1999; *New Scientist*, 2002). However, all deaths in which a post-mortem showed ecstasy to be present in the blood are recorded as caused by the drug, although there may be a variety of other contributory factors. There seems little doubt, however, that ecstasy can sometimes cause death from dangerously high body temperature or by drug-induced liver damage. High doses of the drug administered repeatedly to animals, usually by injection rather than by mouth, can damage the fibres and endings of nerves that contain serotonin and dopamine. In monkeys, doses as low as 5mg/kg injected at 12-hour intervals for 4 days will cause such damage (Fischer *et al*, 1995) – although this is still a very aggressive dose-régime compared with the normal human dose of around 1.5 mg/kg taken by mouth. Nevertheless, some studies have claimed that damage does occur to the serotonin system in the brains of ecstasy users (McCann *et al*, 1998). These results have been given wide publicity, but recent publications have pointed to technical weaknesses in the experiments and their interpretation (*New Scientist*, 2002; Cole *et al*, 2002). The claim that ecstasy use may lead to long-term neuropsychological deficits has also been challenged recently (Cole *et al*, 2002).



SUMMARY

CANNABIS

- Cannabis acts on brain receptors that normally recognize the natural cannabinoid chemical anandamide.
- The active compound in cannabis, tetrahydrocannabinol (THC), cannot be injected and is most efficiently delivered to the brain by smoking.
- Cannabis is safe in overdose, and intoxication does not lead to violent behaviour.
- Smoking cannabis carries hazards of bronchitis and other lung diseases, including possibly cancer – although there is at yet no evidence for the latter.
- There is little evidence that long-term cannabis use damages the brain, immune system or reproductive function, but it can make psychiatric illness worse.
- Approximately 10% of regular cannabis users become dependent, and some may seek treatment.

ECSTASY

- Ecstasy is an amphetamine derivative which combines a stimulant action with mild euphoria/psychedelic properties.
- In overdose it can cause death – 27 recorded in UK in 2000 – although this is low-risk given large numbers of users (estimated at >400,000 every weekend).
- Animals treated with high doses of ecstasy show signs of damage to nerves in the brain containing the chemical messengers serotonin and dopamine.
- Human data purporting to show similar brain damage are contested by some scientists.
- Evidence for long-term impairments of higher brain function in ecstasy users is also controversial.

CONCLUSION

- Both of these drugs seem to fall into the “soft” category – and do not warrant their present Home Office categorizations.

QUESTIONS & ANSWERS

How do we differentiate between hard and soft drugs?
Addictive capacity has to be a major factor in classifying drugs as hard or soft. One out of two people who continue to smoke tobacco throughout their life will die as a result, so this should render it a hard drug in terms of its addictive and lethal potential. However, it is tolerated because it does not impair the ability to work. Heroin is classed as a hard drug, as it is still the most dangerous drug with respect to the number of deaths caused by its acute pharmacological action. Historically opium was widely used and did not elicit the problems associated with the use of heroin today. Now however, it is viewed very negatively by society.

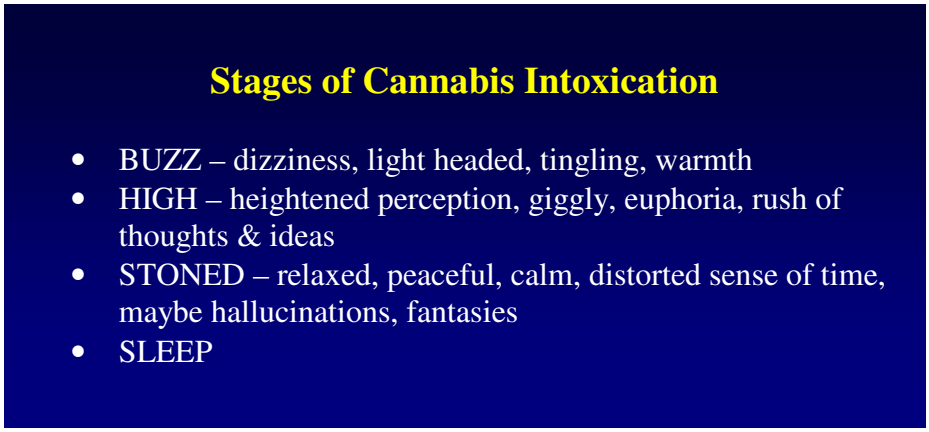
Is cannabis safe when compared to drugs such as alcohol and tobacco?
Versus alcohol and tobacco, it is extraordinarily safe. There are no recorded deaths from overdose or long-term use. Acute toxicity is extremely low. Unlike alcohol, cannabis use does not lead to aggression. It contains the same noxious chemicals found in tobacco smoke, and therefore carries a risk of lung disease. However, some animal studies suggest evidence that it may have a *protective* effect against cancers. Evidence shows that it temporarily impairs certain intellectual functions. There is a reduction in the processing of complex sensory inputs, and executive planning is temporarily impaired. There is as yet little agreement as to the long-term effects of cannabis. Withdrawal in long-term users has been known to impair cognitive function for a few days after stopping. Driving simulators have shown that performance is remarkably good under the influence of cannabis, but this is NOT recommended! The jury is still out as to whether cannabis triggers psychotic illness in those with schizophrenic tendencies, or whether such people use it in an attempt to self-medicate.

Is it possible that people become addicted to the act of smoking rather than to the cannabis itself?
Tobacco is often used when smoking cannabis and people may become addicted to the nicotine. There are also many second-grade reinforcers which have the potential to act as addiction cues, such as rolling papers, special pipes and other equipment.

Why do people talk only about THC (delta-9-tetrahydrocannabinol) when there are at least 50-60 other cannabinoids that have an action?
Only this one major component of cannabis works on the CB1 receptors in the brain. The 50 or so other components may have some weak action on these key receptors but only a fraction of that seen with delta-9-THC. It is these receptors that are largely responsible for the psychostimulant effects associated with cannabis. If these receptors are blocked, the effects of cannabis are not seen. Other cannabinoids act on different receptors and may be involved in modifying the action of THC. They may also have other medicinal effects.

How close are we to legalising cannabis for medical uses?
In Britain the company GW Pharmaceuticals is working on the first medically available THC-based preparation with considerable therapeutic applications, and it could be introduced by 2004. There is also research sponsored by the government

Medical Research Council. The legal use of cannabis derivatives for medicinal purposes is unlikely to be popular with the US authorities, who have denied any medical benefits, and believe it to be a Trojan horse to get cannabis use decriminalised.

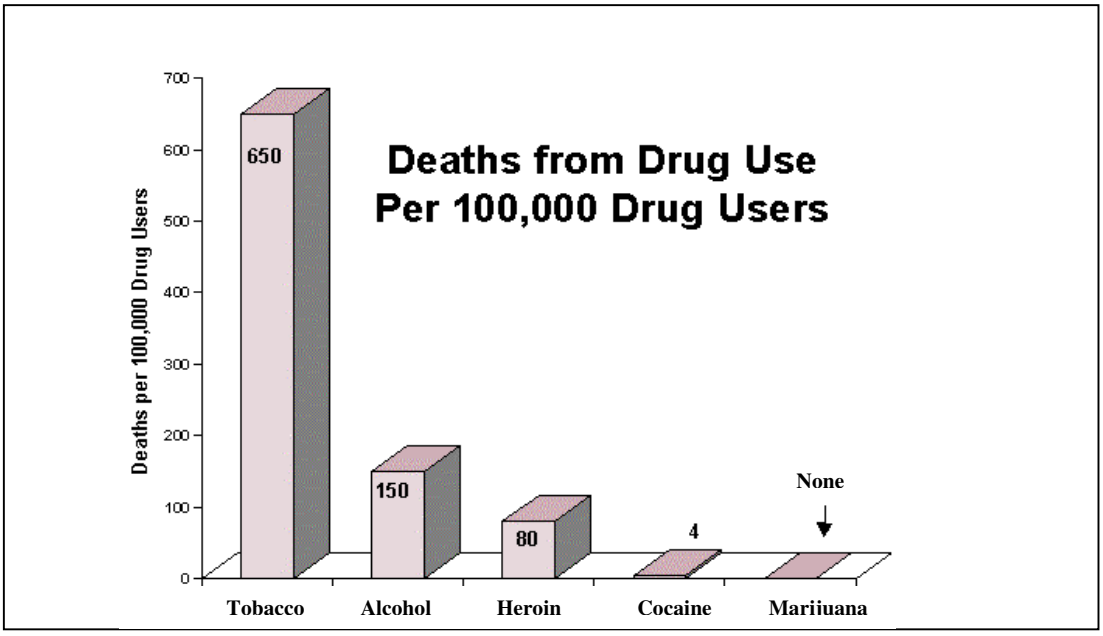


Does the ecstasy that is used for scientific purposes resemble that available in the dance culture?

There is the possibility that drugs available on the illegal market are contaminated. In Holland, quality control is being introduced in clubs. Onsite testing facilities are available, but accurate testing takes time and is impossible to provide instantaneously. Most ecstasy seized by the police has been of fairly high quality.

How good is the evidence for the toxicity of ecstasy?

There is no objective evidence for the destruction of neurons caused by the consumption of ecstasy. There is some evidence that suggests cell damage but also some that contradicts this. We need to remember that scientists are humans as well, and have political/social views that sometimes distort science. There are many examples of sensationalist publications in respected journals, and also many experimental designs which are fundamentally flawed. For instance, a paper in the journal *Nature* concluded that cannabis is as addictive as cocaine - but glossed over the fact that the animals used in the experiments had been trained for years to self-administer cocaine before being switched to cannabis. Another recent paper in the reputable journal *Science* suggested that ecstasy destroyed neurons, but there was no evidence for this destruction. It was necessary to read two-thirds of the paper to deduce that the route of drug administration was injection: 20% of the animal subjects in the experiment died, and another 20% were rendered incapacitated and had to be removed from the experiment – thus suggesting little homology with the real world.



Source: Thinking About Drug Legalisation by James Ostrowsld. Cato Institute Paper # 121

Two Year Test of THC Safety in rats and mice

- Animals treated 5 days a week for 2 years; rats at 50 mg/kg/day, mice at 250 mg/kg/day
- Results were improved survival in treated groups (less cancers) and no evidence of damage to brain or other organs
- Doses equivalent to 500-2500 times human intoxicant dose
- ***[Chan et al. 1996, Fund App Tox, 30:109]***

Canadian Senate Special Committee on Illegal Drugs – Sept 2002

" Marijuana users are unlikely to become dependent. Most users are not at-risk users ... and most experimenters stop using cannabis. ... Heavy use of cannabis can result in dependence requiring treatment; however, dependence caused by cannabis is less severe and less frequent than
dependence on other psychotropic substances, including alcohol and tobacco."

"Scientific evidence overwhelmingly indicates that cannabis is substantially less harmful than alcohol and should be treated not as a criminal issue but as a social and public health issue. We have come to the conclusion that, as a drug, it should be regulated by the state much as we do for wine and beer, hence our preference for legalisation over decriminalisation."