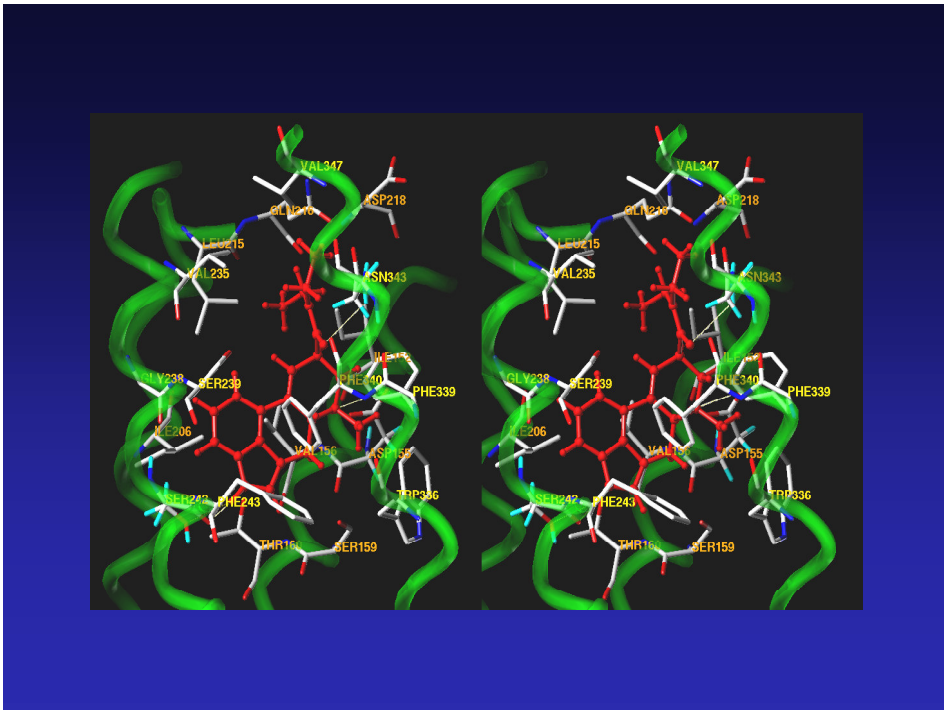
THE BECKLEY FOUNDATION

SOCIETY & DRUGS: A RATIONAL PERSPECTIVE



SEMINAR 1
'DRUGS AND THE BRAIN'

CONFERENCE PROCEEDINGS
MAGDALEN COLLEGE, OXFORD.
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PREFACE

The Beckley Foundation is organizing a series of seminars to address the issue of drugs in society from a multidisciplinary perspective. The first such seminar (Seminar 1), organized in conjunction with Professor Colin Blakemore FRS of Magdalen College, Oxford and Professor Leslie Iversen FRS of King's College, London was held at Magdalen College on 22 October, 2002.

The aim of the series is to encourage a rational overview of the scientific, medical, social and economic issues surrounding the use and abuse of drugs, illicit and legal. Everyone agrees that more informed debate is required as the basis of any further change in attitude and policy. These seminars will therefore bring together leading experts from a wide range of disciplines to examine the latest scientific and professional evidence on:

- The effects of different drugs on the brain, behaviour and health.
- The effectiveness of different methods of informing and educating the public (particularly young people) about drugs and their consequences.
- Issues in the prevention and treatment of addiction, including the relative merits of education and rehabilitation versus penalties and incarceration.
- The likely consequences of decriminalisation and/or legalisation, including issues of regulation and control, implications for public health, law and order and the economy.

Participants at Seminar 1, which was chaired by Professors Blakemore and Iversen, included representatives from the fields of neuroscience, health, education, law-enforcement and policy-making. This Conference Proceedings document summarizes their presentations and the discussions that followed.

Amanda Neidpath

February, 2003

EXECUTIVE SUMMARY

The abuse of illegal drugs, and the criminal activities associated with this, represent a major social and public health problem for all Western societies. The issue of drugs policy is particularly topical in Britain at the moment. The aim of the present series of seminars is to stimulate a rational debate on the options open to policymakers. The first seminar was aimed at communicating some of the latest advances in scientific understanding about how drugs work in the brain - and thus the nature of addiction - to a wider, largely non-scientific, audience.

Alan Leshner, the former Director of the US National Institute on Drug Abuse, effectively conveyed the message that "addiction is a brain disease". There is a fundamentally important distinction between this medical model of addiction, which we subscribe to, and the earlier view of addiction as merely a symptom of moral turpitude. The former can be treated – the latter deserves punishment, and this has tended to dominate society's approach to addicts to date.

Trevor Robbins and **Barry Everitt** reviewed the significant advances that have been made in understanding the brain mechanisms involved in drug addiction. Although addictive psychoactive drugs act initially on a variety of different targets in the brain, the various drugs also activate certain common final neural pathways. These involve the release of dopamine and other brain chemicals, and research has shown that these 'reward' systems are activated not only by drugs, but also by other activities such as sex, food and gambling.

The same reward mechanisms underlie learning and memory. One way of looking at drug addiction is as an aberrant learning process, in which the rewarding properties of a drug become associated with particular stimuli, which then act as 'cues', further prompting the addict to indulge in drug-seeking behaviour to satisfy this new need. Another factor driving continued drug-taking is the desire to escape from the unpleasant symptoms of psychological and physical withdrawal when drug-taking is stopped, and the body and brain are forced into rapid readjustment.

Not all drugs are equally addictive - they vary in their ability to hijack the natural dopamine-dependent learning circuits in the brain. Drugs that enter the brain rapidly are the most addictive, since learning occurs most effectively if two events happen in close proximity in time. Everitt explained that crack cocaine is potentially very addictive because it provides immediate feedback, whereas cocaine taken by mouth acts far more slowly and is less rewarding. In nineteenth century Britain addiction to opium was not common when the drug was taken by mouth, but became common only after the invention of the hypodermic syringe and the injectable opium derivative, heroin. Adults and children treated with the amphetamine derivative "Ritalin" given by mouth rarely become addicted, but amphetamines administered by injection or by smoking can be highly addictive.

Everitt also described recent findings that suggest that the important, dopamine-dependent reward system becomes down-graded in the brains of addicts, suggesting that they need to continue drug taking behaviour in order to maintain sufficient dopamine-related stimulation. An alternative view is that some people have a congenitally poorly-developed dopamine system in their brain, and may therefore be

susceptible to drug addiction as a means of compensating for this deficiency. The question of a possible genetic basis for addictive behaviour remains unanswered.

Robbins and Everitt also stressed the importance of secondary reinforcers in prompting renewed drug-taking. The paraphernalia associated with drug use, the people, place and setting can all act as powerful learned stimuli that can induce a relapse into drug-taking in the reformed addict. The new understanding of these brain mechanisms may help in designing new approaches, both behavioural and pharmacological, to the medical treatment of addiction.

Leslie Iversen addressed the question of whether cannabis and ecstasy should be considered as less harmful "soft" drugs, by comparison with the more addictive and damaging "hard" drugs - heroin, cocaine and amphetamines. The main chemical component in cannabis is delta-9-tetrahydrocannabinol (THC) which acts on a cannabinoid receptor in the brain to trigger the intoxicant effects of the drug. This brain system is normally acted upon by naturally occurring brain chemicals as part of a newly-discovered neural regulatory system. Although a variety of other THC-like chemicals are present in the cannabis plant, none of these appears to be as important as THC.

Many of the earlier health scares attributed to cannabis – that it could impair reproductive function and immune responses and cause permanent brain damage - have not been supported by subsequent research. There are, however, concerns about the damaging effects of smoked cannabis on the lungs, and there is the possibility that, as with tobacco, long-term use could lead to cancers, although this has not been established. Cannabis may also have adverse effects on those suffering from psychiatric illness and the possibility exists that it may precipitate such illnesses in a vulnerable minority. Modern research has also made it clear, contrary to earlier beliefs, that cannabis use can trigger the same changes in brain dopamine mechanisms as other psychoactive drugs, and can lead to dependence in perhaps 10% of regular users.

Nevertheless, by comparison with the legal drugs alcohol and nicotine, cannabis is relatively safe. Overdose does not cause death, and intoxication does not usually precipitate violence or aggression. There are more than 100,000 tobacco-related deaths every year in Britain, and some 30,000 deaths related to alcohol abuse – while none can be attributed to cannabis use. By most criteria cannabis would appear to be a "soft" drug – and the moves by the Home Office to reclassify it into a lower category carrying reduced criminal penalties would appear appropriate. On the other hand, the failure to make any provision for legal sources of supply of cannabis means that users will continue to be exposed to the hazardous underworld of criminal drug dealers, and will purchase a product for which there is no quality control. The Dutch experience in separating the supply of cannabis from that of "hard" drugs is very illuminating, as described at this seminar by the Chief of Police from the Hague (see summary on page 39).

The drug ecstasy (MDMA) is closely associated with the rave dance culture. It presents a more difficult problem of classification. Ecstasy can cause death in overdose – 27 deaths were reported in Britain in 2000, although this number includes every death involving ecstasy regardless of whether other substances had also been taken. It is common for ecstasy to be taken in dangerous combinations with other

psychoactive drugs. However, if the estimate of 400,000 regular users of ecstasy in Britain every weekend is correct, it would have to be considered a relatively safe drug, despite the rare occurrence of fatal overdose. One could argue that no recreational or medicinal drug should be tolerated if it were capable of lethal overdose, but that would rule out both alcohol and aspirin. Ecstasy acts partly as a psychostimulant and partly as a mild hallucinogen. Although there are concerns about the possibility that the long-term use of ecstasy may cause damage to certain neural pathways in the brain, the experimental evidence underlying such claims remains controversial. For the great majority of ecstasy users the drug represents a pleasant diversion from their weekday lives. Placing ecstasy in Home Office Category A – carrying the most severe criminal penalties, has had little effect on consumption to date. The Police Foundation report *Drugs and the Law* (2000) recommended the downgrading of ecstasy to Category B – which would seem to be appropriate, but the Home Office have so far not acted upon this recommendation.

While ecstasy has mild hallucinogenic properties, a curious group of illegal drugs with more pronounced hallucinogenic mind-altering properties were reviewed by **Mark Geyer**. These are known as the "psychedelics", and they include mescaline, psilocybin, LSD and phencyclidine. These drugs are capable of changing brain function in a fundamental way, leading sometimes to new self-knowledge and insights, but also on occasion to nightmare-like experiences. The use of these drugs as possible adjuncts to psychiatry or for military applications was widely researched in the US during the 1950s and 60s, but found little practical application.

The illegal use of psychedelics as recreational drugs sets them apart from most other psychoactive agents, in that they lack addictive properties. The great majority of users do not take such drugs on a daily basis, but only occasionally. Understanding the brain mechanisms which underlie the remarkable effects of psychedelic drugs remains a challenge, although many appear to involve an ability to stimulate brain mechanisms normally activated by the brain chemical serotonin. Little or no systematic research has been done since the 1960s, although current research is beginning to re-open the issue of whether this category of substances may have potential psychotherapeutic uses.

Although intoxication with psychedelics can occasionally lead users to dangerous accidents, for example jumping out of the window in the belief that they can levitate, these drugs on the whole appear to be relatively safe and do not pose any particular danger either to adult users or to society. The wide availability of such powerful drugs to young users, however, is more problematic, because reliable information is not readily available to them. One may therefore wonder whether the psychedelics justify the strict criminal penalties that currently pertain to their use.

David Nutt reviewed the ultimate "hard" drugs – those related to morphine and heroin. These drugs target specific "opiate receptors" in the brain – normally activated by naturally occurring brain chemicals known as "endorphins". Heroin is a morphine derivative that enters the brain more readily, and when administered by injection or increasingly by smoking ["chasing the dragon"] is a highly addictive drug. Addicts suffer a severe physical and psychological withdrawal syndrome if they stop taking the drug, and they run a significant risk of death from overdose. Because illegal heroin is relatively expensive, addiction is often associated with criminal

activity, and the use of contaminated needles helps to spread such viral diseases as HIV, AIDS and hepatitis.

Nutt reviewed the treatments available to assist heroin addicts to quit. An initial period of "detoxification" under careful medical supervision is essential. This is followed by maintenance on some less harmful drug that acts on the opiate receptors in the brain. The synthetic morphine derivative methadone is most commonly used. It is taken by mouth and acts slowly over a prolonged period, helping to maintain the addict and prevent withdrawal. However, it does not give the euphoriant "high" associated with injected or smoked heroin. Newer alternatives include the synthetic drug buprenorphine – already widely used in France. This acts on the opiate receptors but only to produce a partial activation of this mechanism in the brain. While buprenorphine is present in the system the addict cannot obtain further stimulation by taking heroin. Other ingenious ways of preventing the addict from reverting to injectable heroin have also been devised

One radical approach to "harm reduction" is the idea of reintroducing prescription heroin for registered addicts, as was the practice in Britain until the 1960s. At the other extreme of treatment approaches, ex-addicts can be treated with synthetic drugs which act to block the opiate receptors in the brain (e.g., naltrexone). This prevents relapse as the user can no longer derive any pleasurable effects by taking heroin. Most addicts are reluctant to comply with this treatment, unless they are professionals, such as doctors or pharmacists who stand to lose their livelihood unless they can quit their heroin habit. Effective modern pharmacological and medical strategies for treating heroin addicts do exist, but the resources needed to deliver such treatments to those in need are still woefully inadequate. Nutt reported that heroin addicts volunteering for treatment in Bristol had to wait 6 months or more to enter a detoxification programme.

Finally **Michael Farrell** provided some suggestions as to how scientific knowledge of drugs and addiction might be translated into policy and action. He pointed out that drug use in Britain has increased over the past decade, as it has globally. There is a particular problem in the prison population, where almost half the inmates are illegal drug users. A core understanding of the social and biological science underlying drug abuse and addiction is essential in devising a rational and coherent drugs policy. There remains a lack of sympathy for the medical treatment of drug addiction. It is difficult to concede that, as with physical illnesses such as diabetes or multiple sclerosis, the treatment of drug addiction often involves partial remission followed by relapse. Relapse is too often seen merely as moral weakness.

Farrell stressed the urgent need for more research in the under-resourced field of drug abuse and addiction. We appear to rely on the United States to undertake most of the research in this field (more than 80%) with a very well-funded series of programmes. We need more longitudinal studies to measure treatment outcomes, to discuss how to reconcile the probable medical use of cannabis with the continuing illegality of its recreational use, and to devise better pharmacological treatments for cravings. All these are features of what should become an evidence-based approach to the prevention and treatment of drug abuse. If only 1% of the UK budget for drugs policy were expended on research it would increase our research capacity in this field more than ten-fold. The ongoing debate on drugs policy will feature prominently in future seminars in this series.

ABSTRACTS AND SYNOPSES OF SCIENTIFIC PRESENTATIONS

BRAIN MECHANISMS OF REWARD AND ADDICTION

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Many drugs of abuse, including 'stimulants' such as amphetamine and cocaine, opiates such as heroin, cannabis and even 'legal' drugs such as alcohol and nicotine share common features in their mode of action on 'brain reward' mechanisms. Although each of these drugs has a unique molecular target (receptor), and can therefore mimic the actions of several different chemical neurotransmitter systems in the brain, these primary effects of each drug have been shown to influence, directly or indirectly, the activity of a group of nerve cells that use the chemical messenger dopamine. The nerve cells in question are located in the midbrain and send their projections to interconnected forebrain structures including the prefrontal cortex, the so-called 'limbic system' and the striatum.

In studies of animals self-administering drugs (which they do in a manner that is indistinguishable from humans), a ventral region of the striatum, the nucleus accumbens, was found to be the key zone for mediating the rewarding effects of drugs such as amphetamine and cocaine, which directly potentiate dopamine neurotransmission in this structure. Depletion of dopamine from the nucleus accumbens in experimental animals lessened the intravenous self-administration of amphetamine and cocaine, presumably because these drugs had lost their rewarding (or reinforcing) properties. Another key finding was that rats would also self-administer morphine directly into the vicinity of the dopamine cell bodies in the midbrain (where there are many opiate receptors) and that this was associated with marked increases in dopamine in the nucleus accumbens. *In fact, a common effect of stimulants, opiates, cannabis, nicotine and alcohol is to increase dopamine levels in the nucleus accumbens, leading to the hypothesis that the mesolimbic dopamine system has a general role in the reinforcing effects of drugs, perhaps stemming from a more general role in mediating natural rewards.*

Recent studies in healthy human subjects using brain-imaging techniques have shown marked changes in blood flow and dopamine receptor activity in the striatum, not only following administration of cocaine or cocaine-like drugs, but also in response to the expectation of monetary reward. Thus, a popular conception of why people first abuse and then become addicted to drugs is that they increase the activity of a common reward system in the brain, the mesolimbic dopamine system: this is often called a positive reinforcement or incentive view of addiction to drugs, which can be contrasted with a negative reinforcement view that focuses on escape from aversive withdrawal symptoms as primary. Our own view is that drug addiction can best be understood as a pathological subversion of normal brain learning and memory processes, strengthened by the motivational impact of drug-associated stimuli, which leads to the establishment of compulsive drug-seeking habits.

SUMMARY

- Statistics for drug abuse in the UK suggest that cocaine and heroin represent a growing problem. *However, drug abuse is not a simple problem, and abuse of different drugs fluctuates from year to year. It is also difficult to categorise drug abuse precisely because polydrug abuse is the norm.*
- We understand a good deal about how these and other drugs of abuse work in the brain, mainly from experiments with animals.
- In humans the animal data are confirmed by studies using brain-imaging techniques.
- There is probably a common 'reward system' which many, if not all, drugs of abuse appear to influence.
- This reward system includes the nucleus accumbens and the release of the chemical messenger dopamine in this brain structure.
- Drug abuse, addiction and dependence can be considered as aberrant forms of learning, possibly with distinct stages.
- This aberrant learning is controlled by brain structures that interact with the nucleus accumbens such as the amygdala, hippocampus and prefrontal cortex.
- The aberrant learning component of addiction also represents a target for novel treatments (both pharmacological and psychological).

CONCLUSION

- Some areas of the brain, such as the nucleus accumbens, are sensitive to natural (food, sex), conditioned (money) and artificial (brain stimulation, drugs of abuse) rewards: i.e. drugs may usurp or hijack natural reward mechanisms.
- Drugs with apparently different molecular actions may act on the mesolimbic dopamine pathway for their rewarding effects.
- Central to understanding drug addiction is the question of how chronic drug exposure affects the brain and how it responds to this.
- Conditioning mechanisms contribute importantly to addiction and these recruit and devolve control to other brain regions.

QUESTIONS & ANSWERS

The basis of addiction proposed here is a common neural pathway on which drugs act. Why then do some drugs have more addictive potential than others?
Drugs vary in their capacity to affect this common system. Nicotine is less active on dopamine pathways than cocaine or amphetamine, but as addictive. All drugs may affect this common system but also have effects on other pathways. While dopamine action is part of it, other brain areas and neurotransmitters certainly mediate as well.

Why does the use of crack cocaine result in addiction very quickly, whereas long-term use of powder cocaine often does not?
The rate of access of the drug to the brain is a very important factor in how addictive that substance is. Learning works best when two events happen in close proximity in time. If there is a temporal delay between a stimulus and a reward, the association between the two is much weaker. Crack cocaine has a very fast rewarding action, so there is an extremely strong association between the taking of the drug, the paraphernalia associated with it and the rewarding high. Therefore, because of the immediate feedback, crack cocaine is very potent, enhancing the conditioned stimuli (which become cues for drug-taking) through increases in dopamine in the nucleus accumbens.

Is gambling addiction real, or just a sloppy definition?
All addictive behaviours are likely to activate similar parts of the brain. Often we tend to indulge in one single reward to the exclusion of others, although many drug addicts abuse more than one substance. Other behaviours resemble drug addiction with respect to engaging in repetitive activities, but are not identical. For example, obsessive-compulsive disorder is characterised by an increase in the amount of time spent repeating one activity.

Why should the majority of people not seek to maximize their pleasure?
We all seek to maximize dopamine in the nucleus accumbens. Dopamine is like money, it's a basic reward. However, with most people the realisation of the long-term consequences inhibits the taking of immediate reward.

Why do addicts find it so hard to modify their behaviour in the light of its obvious long-term consequences?
The brain mechanisms underlying addiction involve the uncoupling of immediate reward from longer-term consequences. Rats with lesions of the nucleus accumbens will choose small immediate rewards rather than larger delayed ones. Damage to this mechanism leads to a 'here and now' impulsivity. They have lost the ability to mediate delays via learning, so do not think of long-term consequences when making decisions. Similar damage in human drug addicts may result in them choosing short-term highs and failing to take into account the long-term consequences of their drug taking.

Why are humans on the whole able to moderate other types of rewarding behaviours, but often cannot control their compulsion to use drugs?

The great majority of people *can* control their drug-taking, as they do with natural rewards. Others have a lack of control even with natural rewards such as food and sex. Individual variability and genetic predisposition help to explain why some lose control. One brain region implicated in addiction is the frontal lobes that help to regulate the action of the nucleus accumbens. If people are impaired in frontal lobe functioning to start with, there may be an increased probability of becoming addicted. However, the toxic effects of drugs may also target frontal areas and, therefore, drugs may further enhance the drug-taking behaviour through degradation of control mechanisms. Amphetamine addicts often have changes in the frontal cortex that are associated with a loss of self-control.

If both drug and natural reinforcers use the same reward pathways and involve learning, how then can we erase only drug-related memories and not other essential memories?

Reconsolidation is the ability to reactivate memories using reminder cues. It may be possible to activate certain memories using specific cues and then attempt to eliminate these selectively, without damaging an otherwise essential reward system. Protein synthesis encodes and updates memories so we are able to remind a rat of a specific memory and then give protein synthesis inhibitors only when that memory is active. In this way, it is possible to create amnesia for only the specific conditioned stimuli, leaving other reward stimuli intact.

Could there be therapeutic uses for drug action?

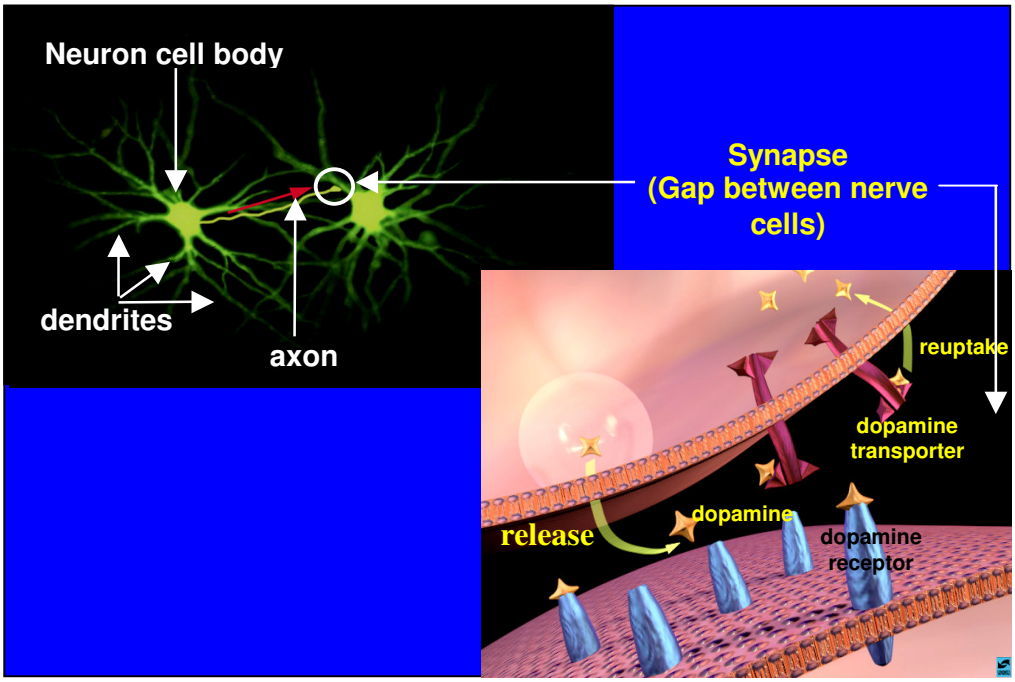
Rehearsing movements can increase plasticity in the brain and cause restitution of damaged areas and/or recruitment of adjacent areas after stroke or head injury. Drugs can strengthen the impact of rehearsed actions, so may be used therapeutically to increase plasticity after damage. There is some evidence that amphetamines can help stroke patients recover, enhancing the rewards gained when movements are rehearsed, and thus reinforcing behaviour.

Illicit Drug Use in the UK: 2000.

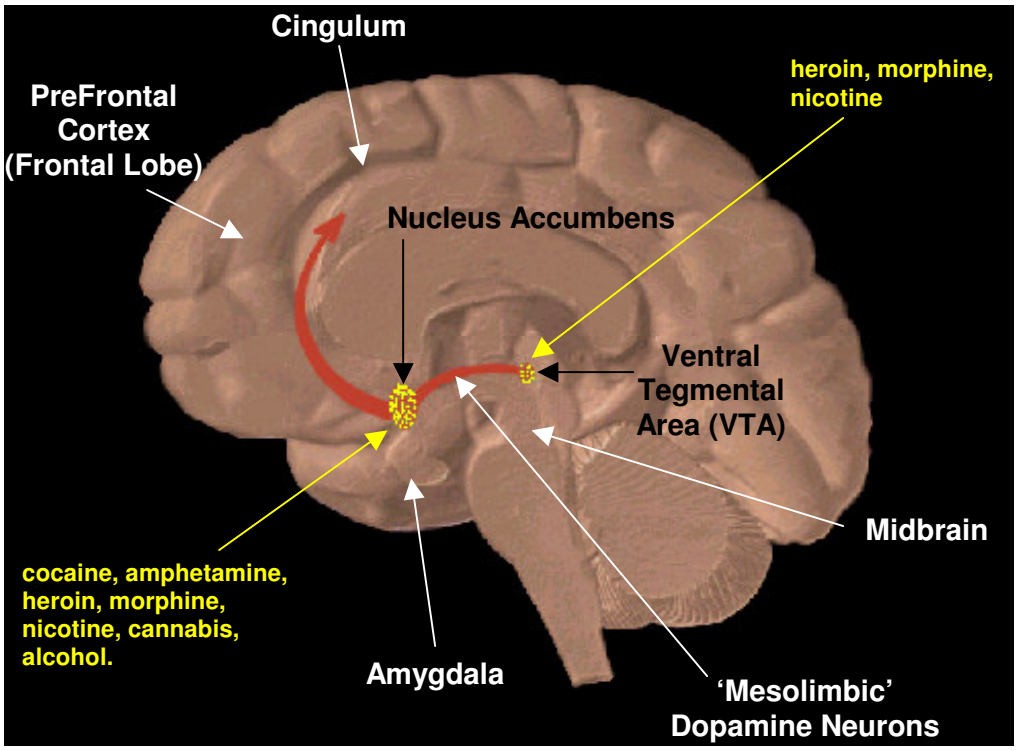
Drug	No. of Users	Annual Value	Popularity
Crack cocaine	210,000	£1,870m	Growing
Heroin	295,000	£2,313m	Growing
Ecstasy	432,000	£294m	Static
Amphetamines	967,000	£258m	Falling
Cocaine*	476,000	£352m	Growing
Cannabis	3,100,000	£1,577m	Static
Total	5,480,000	£6.6bn	

**Use of Cocaine, 16-24 Year olds, up from 1 to 5% between 1994-2000*

Source "Drug misuse declared in 2000: Results from British Crime Survey" (Independent 22/9/2001)



Dopamine Action at the Synapse



Dopamine Reward Pathway Common to All Drugs

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.

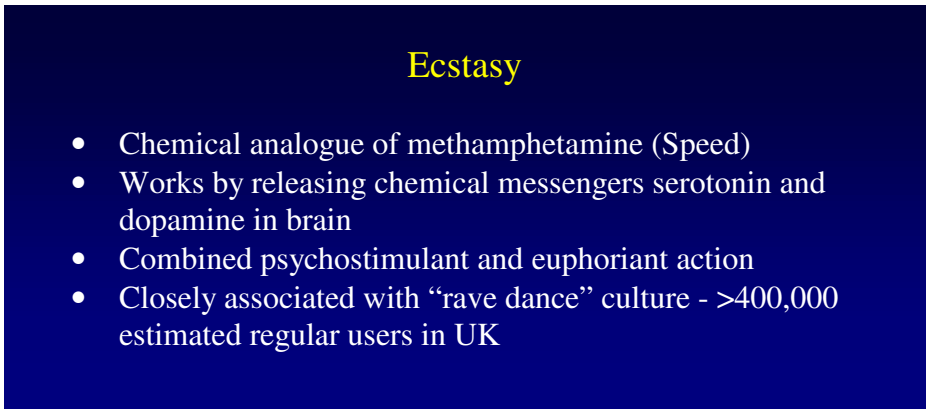
Earlier alarms about the alleged ill-effects of cannabis on reproductive function, the immune system and the so-called "amotivational state" have proved unfounded, as have claims that the drug can cause permanent brain damage. Controversy remains about the relationship between cannabis use and psychiatric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

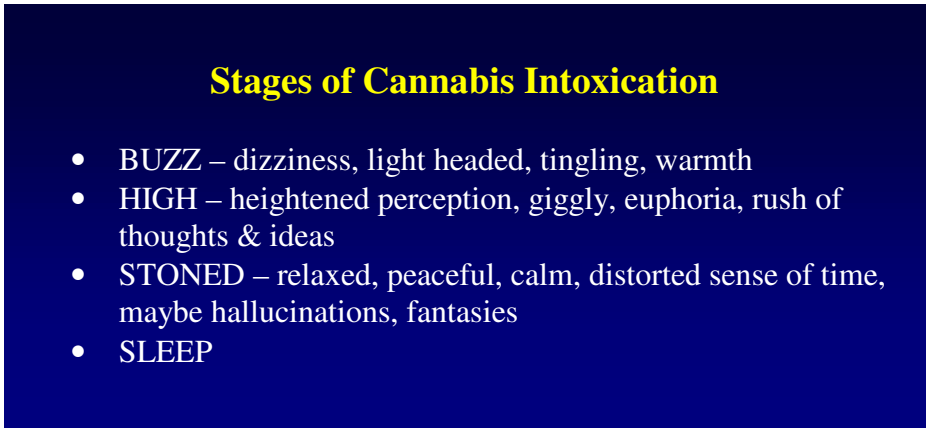
Is cannabis safe when compared to drugs such as alcohol and tobacco?
Versus alcohol and tobacco, it is extraordinarily safe. There are no recorded deaths from overdose or long-term use. Acute toxicity is extremely low. Unlike alcohol, cannabis use does not lead to aggression. It contains the same noxious 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.

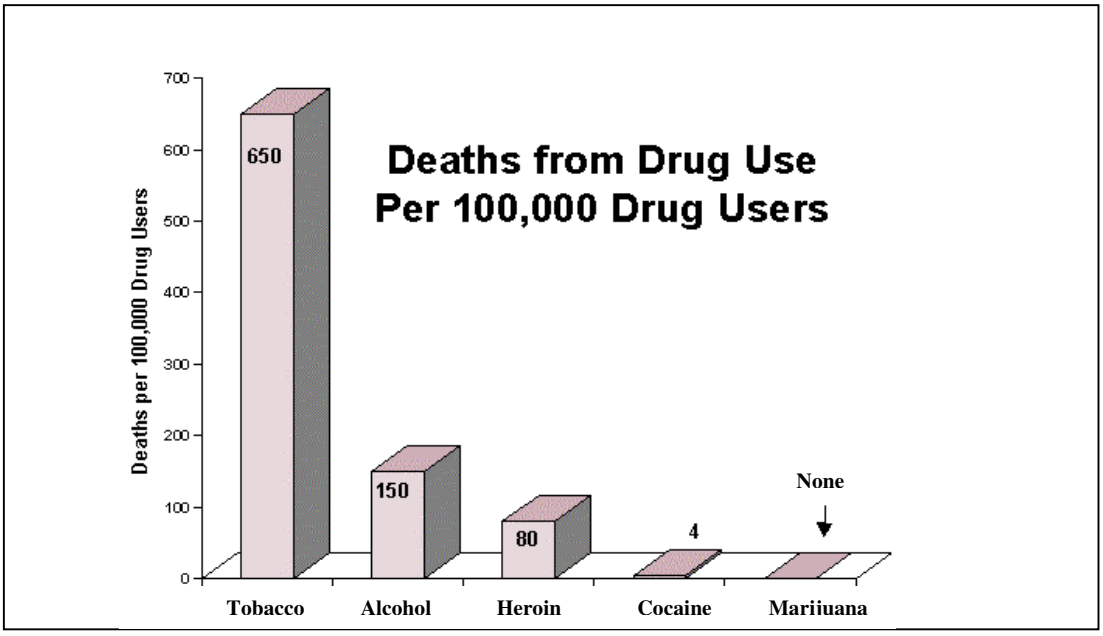


Does the ecstasy that is used for scientific purposes resemble that available in the dance culture?

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."

AMPHETAMINE AND COCAINE – MECHANISMS AND HAZARDS

BARRY J. EVERITT

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Stimulant drugs, such as cocaine and amphetamine, interact directly with dopamine systems in the brain (as well as with noradrenaline and serotonin neurons), and there is widespread agreement that large increases in dopamine in the nucleus accumbens underlie the reinforcing, as well as psychomotor stimulant effects of these drugs. There is also evidence that some of the effects of cocaine and amphetamine show sensitization on repeated drug use, that is, the behavioural response to these drugs increases with drug exposure and this may contribute to the development of addiction. Although there is no physical withdrawal syndrome associated with abstinence from stimulants, there is a 'psychological' withdrawal syndrome that is characterised by dysphoria or anhedonia – depression-like symptoms. Another prevalent view of stimulant addiction is that it is driven by attempts to alleviate the unpleasant effects of withdrawal.

Of special importance is the clinical and experimental observation that otherwise neutral environmental stimuli can become associated with the effects of self-administered cocaine or amphetamine through Pavlovian conditioning. Just as Pavlov demonstrated that a bell associated with food could subsequently, when presented alone, elicit salivation, so cocaine-associated stimuli can have powerful motivational effects. Thus, these stimuli can elicit strong drug cravings, support drug-seeking behaviour and precipitate relapse into a drug-taking habit even in long-abstinent individuals. The behavioural effects of cocaine-associated cues have also been replicated in animal models of addiction, and there are significant similarities between rats and humans in terms of the neural mechanisms that underlie the aberrant learning which contributes to the persistence of addictive behaviour. Reducing the impact of drug cues on craving and relapse is a major novel target of treatments for addiction, and potential pharmacological leads arising from our own experimental work are undergoing clinical evaluation.

Finally, there is some evidence that chronic abuse of cocaine and other drugs, including alcohol, leads to long-term changes in brain function, especially to a decreased activity of the prefrontal cortex. This decreased activity may also contribute to the persistence of addictive habits. Thus, reduced functioning of the prefrontal lobes can disrupt higher brain functions, such as the inhibitory processes that normally hold potentially maladaptive behaviour in check. Some of the behavioural and cognitive characteristics of drug-abusers – including impulsivity, risk-taking and apparently poor decision-making abilities – resemble effects of damage to the frontal lobes. We have shown that chronic amphetamine-abusers show deficits in their decision-making abilities that closely resemble those seen in subjects with orbital frontal lobe lesions. Therefore, chronic abuse of cocaine, amphetamine and perhaps other addictive drugs may impair brain function in a way that contributes to the persistence of addictive behaviour.

SUMMARY

- Cocaine and amphetamine predominantly block re-uptake of dopamine in the nucleus accumbens, hence more dopamine is available in the synaptic cleft .

- Environmental stimuli become associated with the effects of self-administered cocaine or amphetamine through Pavlovian conditioning. These environmental stimuli subsequently elicit craving, drug-seeking and relapse. Treatment may be able to target drug cravings by reducing these secondary cue motivations.

- Aberrant learning contributes to the persistence and gravity of addictive behaviour, and may be a significant cause of relapse in addicts.

- Addicts show impairment of executive functions, for example: impulsivity, poor decision-making, decreased capacity to inhibit inappropriate behaviour and thus reduced self-control.

- Adaptive consequences of chronic drug usage may reduce the decision-making abilities of users by inducing changes in the prefrontal cortex, which are likely to impact on cognitive processes. On a behavioural level, these changes can cause the persistence of maladaptive drug-taking.

- Alternatively, addicts may begin to abuse drugs in the first place due to their pre-existing poor decision-making abilities, which could result from damage to the prefrontal cortex. In other words, damage to the prefrontal cortex may predispose individuals to addiction.

- Novel treatments may be able to act prophylactically to prevent drug cues eliciting relapse and drug-seeking behaviour.

CONCLUSION

- More research is needed into the neurophysiological changes which accompany addiction, in order to provide a greater understanding of addictive behaviour and the predisposition to it.

- Pharmacological and behavioural approaches need to be developed that aid the extinction of reinforcing cues.

QUESTIONS AND ANSWERS

How can we relate scientific findings to more socially-orientated studies?

We may be able to identify mechanisms of drug-taking persistence, and on the basis of these develop treatments. If the underlying mechanisms can be identified, suitable interventions can more readily be developed. People will always experiment with drugs, and we need to understand the mechanisms that can turn use into abuse, and that may finally lead to addiction. It is also important to remember that some abusers die, so any findings with potential applications must be investigated, as they could potentially save lives.

Are certain people more vulnerable to addiction and can they be identified?

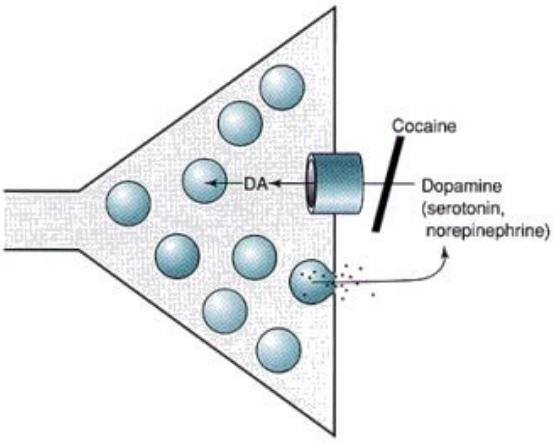
There is no single picture of an addictive individual. There are many people who use cocaine for years without becoming addicted. Some people become addicted and some do not. The finding of low density of dopamine receptors in drug-users could be interpreted as these people having *congenitally* low levels of dopamine receptors, which tends to make them seek a way to self-medicate by taking drugs. Primate studies show subordinate animals have low levels of dopamine receptors, and this predicts their drug-taking behaviour. This is an area that we need to explore in much greater detail.

What are the effects of stopping drug use?

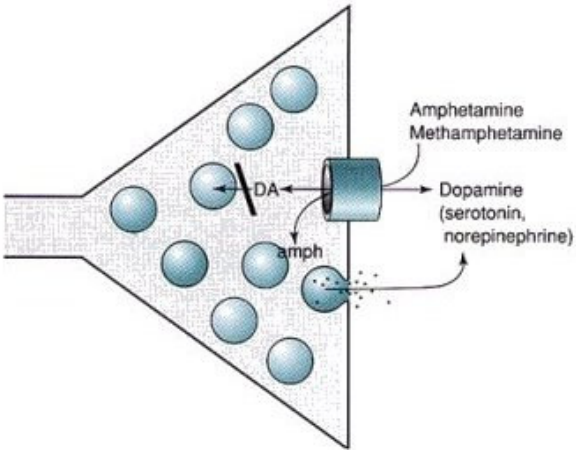
After stopping drug use, there is a reduced availability of dopamine receptors in the striatum and decreased dopamine in the nucleus accumbens, leading to symptoms similar to depression. Studies on glucose metabolism, (which is an indirect way of looking at brain activity) show that 100 days after stopping chronic cocaine use, frontal cortex activity is still reduced, executive functions are impaired and there is a reduced ability to control bad habits. Tests of cognitive functions in amphetamine users have shown poor results. Damage to the pre-frontal cortex can predispose animals to take drugs.

Why are treatments for dependence so ineffective?

Pharmacological treatments have tended not to be developed because there has been some stigma attached to treating addicts. Additionally such drugs may not be considered economically viable by pharmaceutical companies. Methadone and nicotine patches are drug substitutes, keeping addicts off more harmful drugs during a slow withdrawal process. Pharmaceutical companies are only just beginning to be interested in drugs that act as abstinence aids rather than as substitutes. Many treatments have serious side-effects. Treatment and harm reduction must be used conjointly.



(A) Cocaine inhibits dopamine re-uptake (also re-uptake of noradrenaline and serotonin)



(B) Amphetamine enhances dopamine release (also release of noradrenaline and serotonin)

Conditioning and Psychomotor Stimulant Addiction

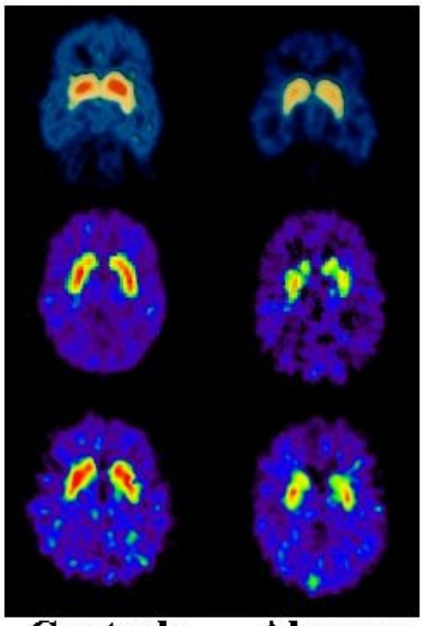
Environmental stimuli become associated with the effects of cocaine and amphetamine through Pavlovian conditioning

Dopamine D2 Receptors are persistently decreased in the brains of addicts

COCAINE

METH

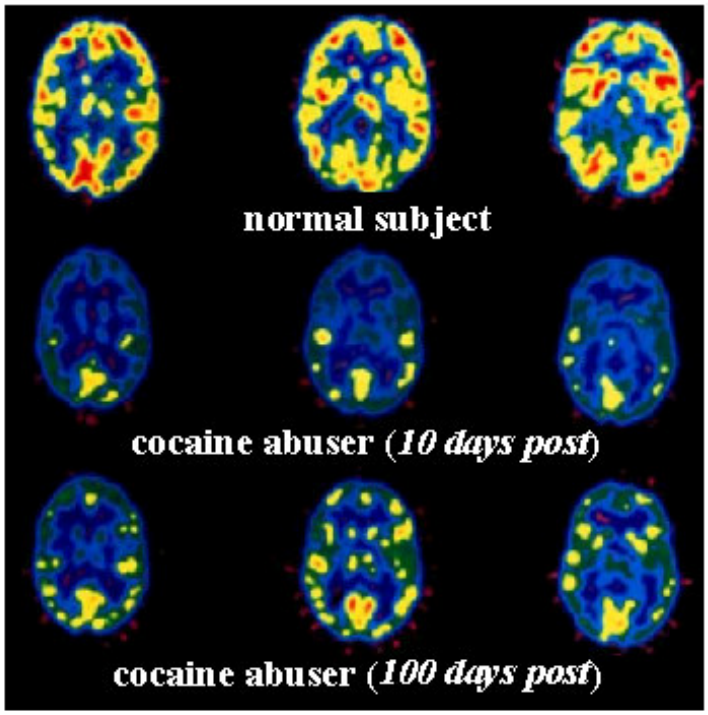
ALCOHOL

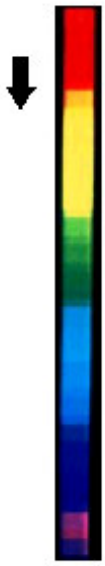


Controls Abusers

Volkow et al., 1999

Cocaine Abuse and Brain Glucose Metabolism





Volkow et al., 1998

HEROIN AND RELATED OPIATES

DAVID J. NUTT
Psychopharmacology Unit, Bristol University

Heroin is a derivative of morphine and both belong to a large family of drugs called the opiates, that were originally extracted from the resin of the opium poppy and which have been used by humans for millennia. They have strong pain-relieving actions and play a prominent role in the management of severe traumatic and post-operative pain, as well as in terminal care. When used in other circumstances, their profound ability to produce a state of inner tranquility and euphoria can lead to their misuse. Addiction to opiates is due to the often overwhelming desire to re-experience this mental state, and on repeated use many individuals become physically dependent on these drugs. This dependence leads to an unpleasant and sometimes dangerous withdrawal state when drug use is stopped, and the avoidance of this withdrawal helps to maintain drug use.

Opiate painkillers include drugs such as morphine and heroin, as well as the much-used codeine and powerful synthetic analgesics such as fentanyl and buprenorphine. In the brain there are a number of pathways in which endogenous opioid peptides (the endorphins and enkephalins) act as transmitters. Opiate drugs act on the same receptors as natural opioid peptides, but in some circumstances they can produce excessive stimulation of these receptors, leading to great pleasure but also a great risk of dependence and addiction.

Many factors increase the risk of opiate addiction, but the most important factor is the speed with which the opiate gets to the receptors in the brain. Over many centuries of use there has been a series of developments to produce opiates that get into the brain ever more rapidly. Heroin itself is a version of morphine designed to enter the brain faster, but once there it is converted back to morphine. Other ways of accelerating brain-entry involve bypassing the gastrointestinal tract. Taking opiates by smoking or by the intravenous route gets the drug into the blood and brain very quickly, producing much higher levels of stimulation for a shorter period. This pattern of extreme peaks and troughs of opiate action in the brain underpins many aspects of addiction, including the intense degree of craving and drug-seeking behaviour. Intravenous use is also a major cause of secondary illness, especially infections such as hepatitis and HIV.

Understanding of the pharmacology of opiates has helped design and optimize interventions for the treatment of addicts. Some, such as methadone, replace the chaotic use of heroin with the controlled and regulated use of a similar drug, with a longer brain action and a better use profile. Other drugs, such as naltrexone, act to block the effects of heroin in the brain, so making its use pointless. However, the low acceptance of this approach by street addicts means that it is rarely used except in special patient groups such as doctors and pharmacists. Buprenorphine is a new drug that acts partially like an opiate to encourage compliance with treatment and partly like an antagonist to block the effects of heroin should it be taken on top. It has become the main treatment of heroin addiction in France, and is now being used in the UK.

SUMMARY

- Heroin is easily classified as a hard drug because repeated use often leads to physical dependence and there is a dangerous withdrawal syndrome. Also, overdose can cause death.

- The degree of addictiveness is determined by the speed at which the opiate gets to the receptors in the brain. Therefore, smoking or intravenous use of heroin often leads to addiction, while oral use of opium derivatives poses less of a problem.

- A pattern of peaks and troughs of opiate action in the brain contributes to the craving and drug-seeking behaviour that characterise addiction.

- There are considerable risks related to the route of drug administration. Intravenous use can result in overdose and lead to infections such as hepatitis and HIV. There is virtually no risk of overdose with smoking, but there are risks associated with lung damage.

- There is a potentially lethal dose threshold with full agonists like morphine and heroin. Partial agonists like buprenorphine blunt the activity of the full agonist, making it impossible to exceed this threshold.

- Methadone is used as a heroin substitute rather than a treatment.

- Antagonists like naltrexone stop the agonists working completely, but they are not popular with addicts because they have not even partial heroin-like effects, unlike buprenorphine.

CONCLUSION

- A growing understanding of opiate action is leading to the development of better treatments. Currently several different combinations of agonists and antagonists are being developed, in an effort simultaneously to improve compliance and reduce heroin use.

QUESTIONS AND ANSWERS

What are agonists and antagonists?
Agonists are chemical substances which act to mimic and enhance the action of naturally occurring chemicals in the brain. Antagonists act to block the action of such chemicals on the brain's receptors.

How are antagonists used to block the effects of heroin?
Naltrexone is generally taken orally on a daily basis, but it can be implanted under the skin. It blocks the effects of heroin completely. However, individuals experiencing trauma can still be treated for pain whilst taking naltrexone, as some painkillers and anesthetics are still effective. Naltrexone does not block the effects of cocaine.

What are the ethical challenges associated with making conformance to treatment with an antagonist a bail condition?
There are other examples of similar bail conditions that are considered ethical. For example, drink-drivers are offered incentives (shorter ban/smaller fine) if they agree to attend alcohol-dependency programmes and educational courses. The drawback is that most medications only work well with compliance, and those addicts who are willing to comply are likely to be those that least need to take medication to come off the drugs.

There are severe ups and downs associated with the use of heroin. Do those who take heroin and manage to live productive lives still have these same usage kinetics?
All heroin users will experience the highs and lows of addiction over a similar time course, but controllability is a major factor. Some users can maintain a productive life with less marked downs, due to maintenance of supply. The fear of withdrawal increases the motivation for the drug, so the user will seek it more desperately. Maintenance of supply lessens the compulsive behaviours associated with satisfying the habit, thereby cutting crime and unproductive preoccupations.

Is it a good idea to prescribe heroin to addicts?
The Dutch and Swiss experiments suggest that there are benefits to the individual, but with costs to society because of the expense of "shooting galleries." The question is not whether shooting-up is bad, because it obviously is, but whether it is more cost-effective than other methods of treatment. Preventing people fighting and stealing to feed their habits is bound to be beneficial to society but there are other factors, such as cost, involved in its potential as a treatment. To make it less expensive a 'take-home' arrangement is needed, so that addicts come in only once a day for the dosage and then do the rest at home. However, this option has generally been considered politically unfeasible. Some have recommended that for certain individuals the use of prescribed heroin can be the best treatment.
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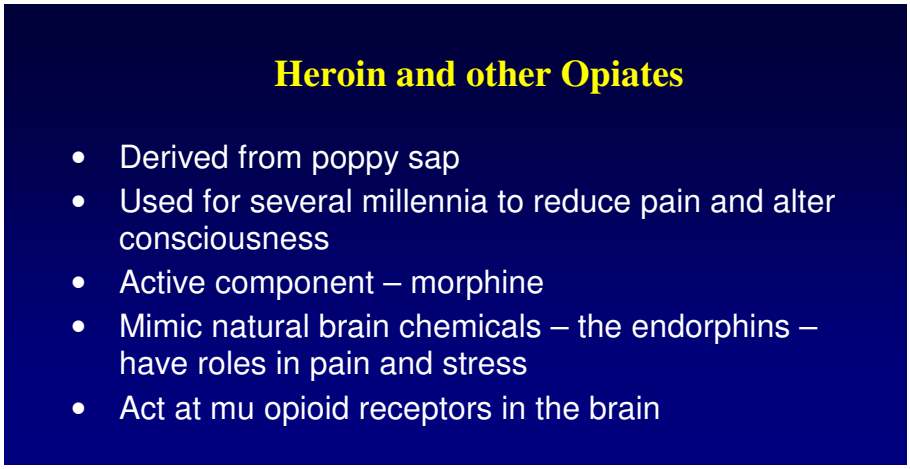
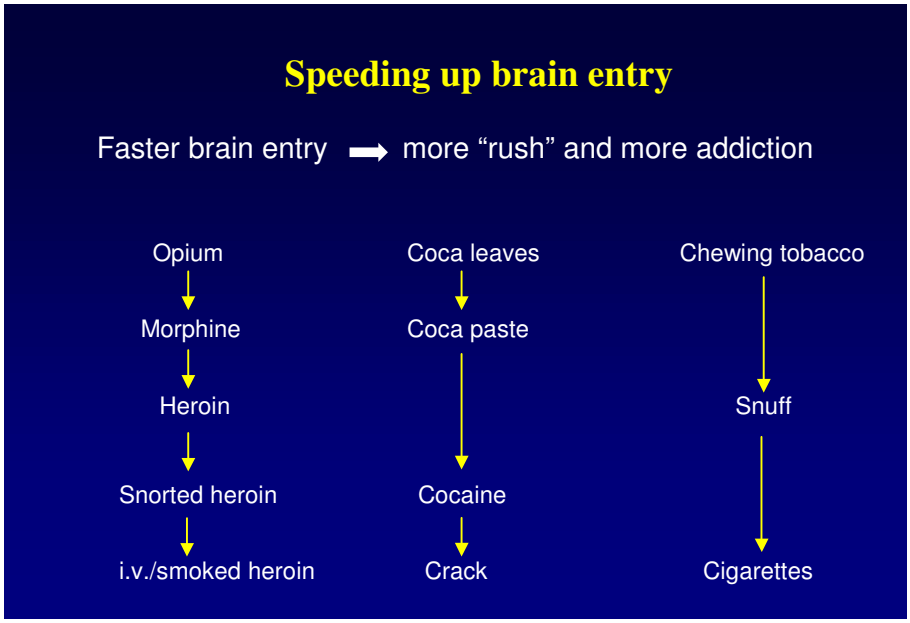
Is the vaporisation of diamorphine a potential treatment for heroin addiction?

It is virtually impossible to overdose by smoking, but there is likely to be some lung damage. If the heroin is pure, smoking is the preferred means of administration by users. However, due to the impurity of illegal drugs, many addicts prefer to inject as smoking the impure substance is ineffective. It is very difficult to get addicts who are used to injecting to switch to smoking. Once the IV route has been experienced, secondary reinforcers become so powerful that it is difficult for addicts to go back to the inhalation route.

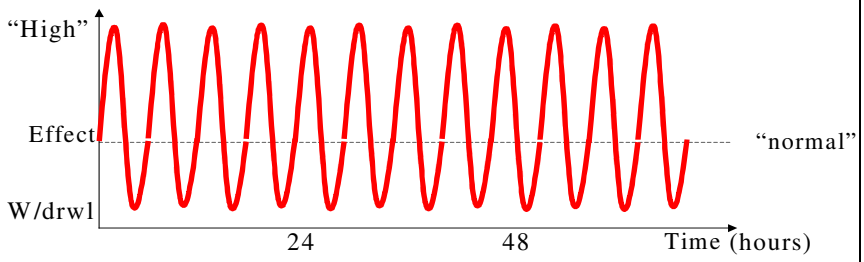
What is the role of opioid receptors in addiction?

Studies have shown a relationship between the degree of cocaine-craving and opioid receptor activity. Endogenous opioids may well be important mediators of the addictive potential of other drugs, including cannabis.



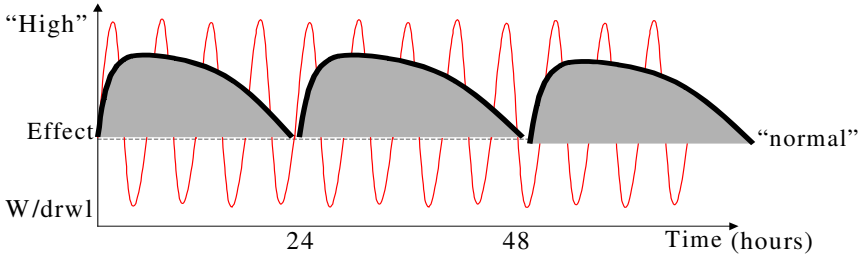


Heroin - dosing principle



Heroin – short half life means brain levels fall fast so user loses effects and gets withdrawal → repeated use

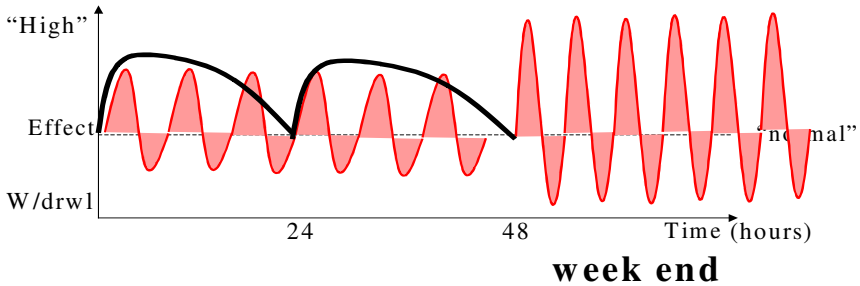
Slower kinetics → reduced abuse



Methadone

- **slower to peak → less rush**
- **slower offset → less withdrawal**

Methadone blocks "on top" heroin



week end

Methadone

- **when in brain blocks actions of heroin**

PSYCHEDELICS

MARK A. GEYER

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Mankind has used psychedelic drugs for thousands of years. Originally, plant materials were discovered by many peoples to have the psychoactive properties now associated with known and often synthetic chemicals. In many ancient cultures, the use of these plant materials became incorporated into religious beliefs and practices, with the plants becoming sacraments used ceremonially and medicinally. Some of these sacramental practices continue to this day and are legally sanctioned.

In modern Western science, both the active components of plant materials and newly-synthesized psychedelics have been identified and studied. The isolation of mescaline and psilocybin as the active principals in peyote and magic mushrooms respectively, coupled with the discovery of the activity of lysergic acid diethylamide (LSD) and the synthesis of phencyclidine, has led to the recognition of four main chemical classes of psychedelics. Although each class exhibits unique pharmacological effects, the three types of classical hallucinogens that share major mechanisms of action are the phenalkylamines such as mescaline, the indolealkylamines such as psilocybin, and the ergot alkaloids such as LSD. The more psychotomimetic class of compounds, the NMDA antagonists exemplified by phencyclidine or ketamine, includes dissociative anaesthetics that produce a different profile of effects, overlapping to only a limited degree with the effects of the classical psychedelics.

The psychedelics differ from most other drugs that have been regulated by modern Western cultures as being “drugs of abuse”. The most striking difference lies in the typical pattern of use of these drugs. While virtually all other legally defined drugs of abuse generally lead to frequent and uncontrolled consumption in humans and are self-administered by experimental animals, psychedelics are almost always ingested only occasionally by humans and are not self-administered by either rodents or monkeys. Coupled with the absence of any notable withdrawal phenomena associated with discontinuation of psychedelic exposure, these patterns of use indicate that the psychedelics are not “addictive” by virtually any definition of the term.

Scientific research regarding the nature and neurobiological mechanisms subserving the effects of psychedelics flourished briefly after the chemical identification of specific compounds and, especially, the discovery in 1943 of LSD. However, the societal disturbances associated with the widespread popularity of psychedelics in the 1960s led to their legal control and a cessation of most scientific investigations. The tremendous advances in basic neuroscience, and the recognition of the importance of drugs acting on serotonin receptors in the treatment of psychotic disorders, has prompted a revitalization of research involving these compounds in recent years. As a result, important new information is now available regarding the neurobiological systems involved in the profound behavioral effects of psychedelics in humans as well as in experimental animals, with a particular focus on the

neurotransmitter serotonin as a key player. The new insights drawn from this research have important implications for both the treatment of psychotic disorders and for the potential psychotherapeutic uses of the psychedelics themselves.

SUMMARY

- Historically, psychedelic plant extracts have been used as religious sacraments. These traditions have been modernised by the use and production of LSD.

- There are three types of classical hallucinogens that share major mechanisms of action: the phenalkylamines, the indolealkylamines, and the ergot alkaloids.

- Psychedelics are not addictive - animals do not self-administer these drugs and humans who use them do so intermittently - a rapid tolerance stops continued use. Furthermore, there are no withdrawal symptoms.

- There is no strong evidence that the use of hallucinogenic drugs induces psychosis. Psychedelic states may resemble the very early stages of schizophrenia, but do not resemble the syndrome. Lasting psychoses appear to be associated with a predisposition to schizophrenia. Few enduring effects are seen in animals.

- Due to a lack of official support, there has been a poverty of research into the potential therapeutic applications of the psychedelics. There is little interest from drug companies as small doses are likely to be used on a one-off, or very infrequent basis, and such a limited therapy would not be financially viable for them.

- Serotonin has been identified as a key mediator of psychedelic action. There are different physiological mechanisms associated with serotonin receptor activation underlying different sets of the behavioural experience.

CONCLUSIONS

- Psychedelics are ancient medicines that have received little scientific attention.

- Psychedelics are not addictive.

- Further studies could increase our understanding of a variety of mental states and potential therapeutics. Therefore, more research needs to be done on this very interesting category of compounds.

QUESTIONS AND ANSWERS

How do the effects of psychedelics compare to other recreational drugs?
Out of all the recreational drugs, psychedelics have the most profound effects on information processing and self-identification. LSD is not addictive and there is no evidence that its use leads to a crime industry, so regulating use would not be a burden on society. The setting dictates the type of effect, which is not as predictable as other drugs. In the subculture a system of supervision has evolved naturally, which includes management, guides and safety issues.

Is there a potential for people on psychedelics to do dangerous things due to the intensity of their highs and visual distortions?
There is a risk of doing something that may harm the drug user, for instance a distorted belief in the ability to levitate may lead a person to jump out of a window. However, there have been relatively few reported incidents. The use of LSD in vulnerable individuals without supervision can be dangerous, as 'acid trips' are extremely unpredictable. The risks can be minimised if the drug is taken in a safe environment with a mentor-type figure or a reliable companion. It is important for users to be educated about the effects and potential risks. Unfortunately, use is often in the hands of the least educated.

Are there constitutional and contextual determinants of which classes of symptoms are experienced?
With respect to constitution, all the available evidence is anecdotal. However, it is likely that some individuals are more susceptible to paranoia than others. Contextual determinants are very significant. Ken Kesey (author of 'One Flew Over the Cuckoo's Nest') obtained access to experiments of the CIA in which LSD was tested as a possible agent of war, mind-control and interrogation. The studies revealed that 'bad trips' were much more likely when the user was unaware that they had taken the drug. This stems from an inability to attribute their strange experiences to the effects of the drug.

Can we learn from the treatment of psychiatric patients with psychedelics?
Psychedelics were used in America in the 1960s and in Switzerland up until the 1990s to treat patients suffering from a variety of mental and physical illnesses. Psychedelics were found to help some cancer patients accept the fatality of life, and reduced their dependence on morphine. These drugs also showed potential therapeutic uses for overcoming alcohol dependence.

Legally Defined Hallucinogens

- Classical hallucinogens = Psychedelics
  - Mescaline, psilocybin, DMT, LSD
  - serotonin (5-HT-2A) agonists
- Dissociative anesthetics
  - PCP, ketamine
  - NMDA antagonists
- Marijuana, THC
- Entactogens
  - MDMA, a-ethyl-tryptamine
  - serotonin releasers

What are Psychedelics?

- Ancient medicines and religious sacraments derived from plants
- Modern synthetic compounds used "recreationally"
- Defined by human reports of alterations in
  - consciousness, perception, thinking, mood
  - experiences of the self and environment
  - contemplative and religious exaltation

Kernos Vessel for the Eleusinian Ceremony

From ca. 1500 BC until ca 400 AD

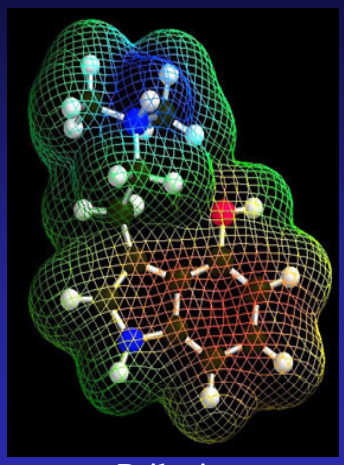
Potential Therapeutic Applications

- Use in Obsessive-Compulsive Disorder
- Body dysmorphic disorders (e.g. Anorexia)
- Cluster headaches
- Convict rehabilitation
- Alcohol and substance abuse
- Relief from intractable pain
- Depression in terminal illness

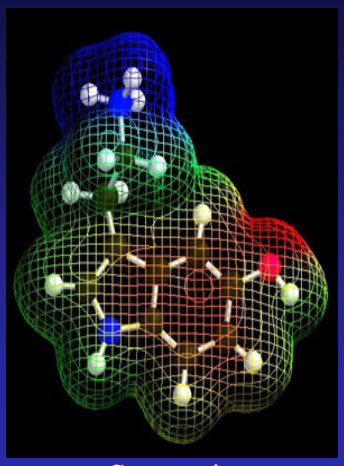
Areas of Potential Interest

- Theories of mind and consciousness
- Sensory processes and cognitive functions
- Structure & development of personality
- Processes involved in dreaming
- Exploration of meditative states
- Parallels to near death experience
- Theories of spirituality - "Entheogens"
- Models of psychoses - "Psychotomimetics"

3-Dimensional Structures of Psilocin & Serotonin

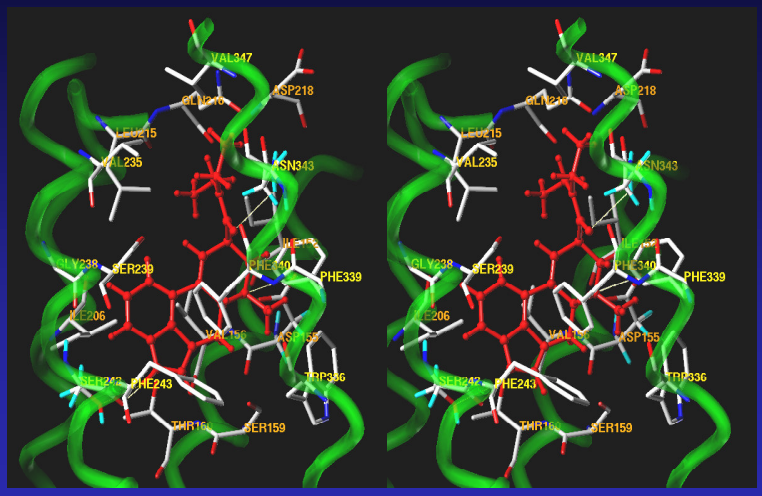


Psilocin



Serotonin

Convergent Stereoview of LSD Docked into h5-HT$_{2A}$ Receptor



Images provided courtesy of the Heffter Research Institute

How Can We Translate Science into Policy and Action

Michael Farrell

Consultant Psychiatrist, National Addiction Centre

There has been a trend towards increased drug use over the last ten years. Making the link between science and policy is a major challenge, yet necessary to provide a better understanding of the effects on society. A core understanding of the social and biological sciences assists in pursuing an informed and coherent drugs policy. Understanding the differing properties of the various drugs available can highlight the necessity to have different policies for different drugs. Also, understanding some of the core scientific findings behind the biological mechanisms underlying dependence can assist in planning responses and therapies.

The National Institute on Drug Abuse in the US has promoted the concept of "addiction as a disease of the brain", arguing that such an approach can improve the public understanding and sympathy for those with drug induced disorders, and that this in turn can promote investment in research and development of new treatments for addictive disorders. However, there is less sympathy for this approach in Europe.

Overall 80% of funding for drugs research is expended in North America. It can be argued that if 1% of the total budget for drugs policy in the UK was spent on research, it would increase the research capacity of the field by over 10-fold. Such an investment is a critical component of an approach to developing a more rational and effective drug policy for the coming decade.

Ever and past year drug use in 16-35 yr olds

	Ever used		Used in past year	
	1993	2000	1993	2000
Cannabis	19.6%	45.2%	8.3%	20.9%
Cocaine	1.8%	9.2%	0.4%	4.2%
Amphetamines	5.0%	15.1%	1.8%	4.8%

SUMMARY

- There has been a substantial growth in the number of people who have ever used and recently used illicit drugs. Drug-dependence is especially prevalent in prison occupants.

- Both public and political opinion is subjective and very influenced by the media. Only carefully controlled scientific research on the neurophysiological action of drugs is objective and should form the basis for policies.

- Europe has not been keen to adopt the view of "addiction as a disease of the brain".

- Compliance and relapse rates when treating drug addiction are similar to many other conditions, such as asthma, hypertension and diabetes. Because these chronic conditions are susceptible to repeated relapse, any treatment has to have a longitudinal dimension to it.

- Social and cultural issues must be considered and tied in with scientific understanding in order to produce an informed policy that is also practical and achievable.

- Research in the UK is severely under-funded compared to the US, and this discrepancy needs to be addressed.

CONCLUSION

- Problems associated with drugs continually change as different drugs gain popularity.

- Science and research must focus on the different problems which arise from different drugs in order to provide a better understanding and make the case for more rational responses.

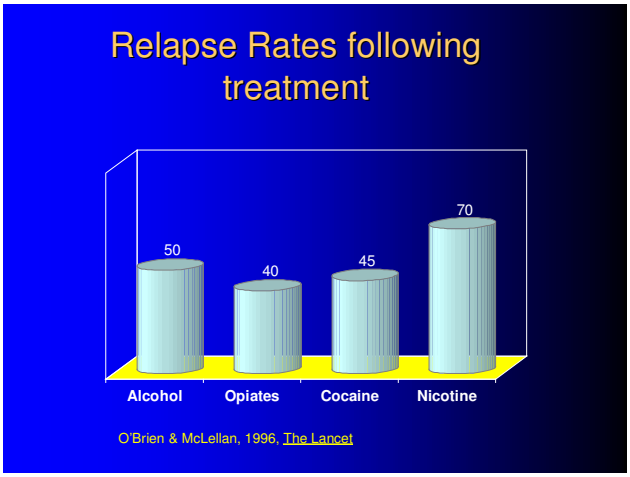
- More investment is needed for research on drug addiction and the potential therapeutic uses of these substances.

- US drug policy dominates worldwide, despite issues in other countries being very different.

- We need a better understanding of how drug use and abuse affects our society. It is necessary to establish links between what needs to be done socially and the scientific findings and treatments being developed.

SUMMARY OF KEY INFORMATION OUTLINED BY PREVIOUS SPEAKERS

- Drugs of abuse activate a common reward pathway.
- Learning is a very important component in drug addiction.
- What fires together wires together.
- Most drug abusers are polydrug users.
- Addiction favours immediate versus delayed rewards.
- It is important to provide accurate information to the public.
- We need better pharmacological and behavioural treatments for addiction.
- Cravings can be modified through dopamine receptor modifications.
- Need for open discussion on use of cannabinoid agents for possible therapeutic uses.
- Need more longitudinal studies on effects of drug abuse because relapses are very common.
- Need for better understanding of functional use of drugs of abuse.
- Need for an evidence-based approach to prevention and treatment.
- Need for improved access to treatment.
- Current US style policy dominates despite issues being different in different countries.



9 Year old in Thailand

In Asia there is currently an explosion of methamphetamine abuse

JAN WIARDA - HEAD OF POLICE, THE HAGUE
&
BOB AINSWORTH - MINISTER IN CHARGE OF DRUGS POLICY IN THE UK

Among the participants were Jan Wiarda and Bob Ainsworth who were kind enough to give presentations as a supplement to the scheduled scientific program.

JAN WIARDA

HEAD OF POLICE, THE HAGUE

MAIN FEATURES OF THE DUTCH POLICY ON DRUGS

- In the Netherlands the possession of drugs is illegal, but the *use* of drugs is NOT.
- Dutch legislation is consistent with the provisions of all the international agreements.
- The main aim of Dutch drugs policy is *harm minimization* – i.e., to minimize, if not prevent, harm to users, the people around them, and the public in general.
- The Dutch policy aims to prevent, or at least limit, the risks associated with drug use. The fact that users are not prosecuted, or stigmatized, makes it easier for them to seek help.
- The Dutch experiment started in the 1960s. Initially it was resisted, but in time it was accepted as people from all walks of life saw their children try cannabis and observed that its use generally did not progress on to the use of hard drugs.
- There is hardly any problematic cannabis use, and no reported casualties related to cannabis products. The long-term effects are less known at this stage.
- There is no evidence that the policy on soft drugs encourages the use of hard drugs and only a very small percentage of soft drug users change to hard drugs. An increase in the use of ecstasy parallels that seen in other countries and is unrelated to Dutch policy on drugs.
- Coffee shops found selling hard drugs are closed down immediately.
- The one major ambiguity in the system is that the supply to the coffee shops is not regulated and criminal organisations are still producing, transporting and distributing marijuana products.
- Ideally there would exist an official, closely regulated, closed market supply in the Netherlands. The revenue from taxes would go to pay inspectors to check quality and prevent it from being exported. However, international obligations led by the US do not allow it, so the ambiguity remains.
- Dutch policy on law enforcement and prosecution is set out in official guidelines, so is very transparent. It encourages a lot of teamwork between the police, judicial authorities, social work and the medical sector.

- Treatment has been found to be much more effective than detention, so it is supported. Drug addicts who are offenders are encouraged to have treatment and thereby suspend or waive their sentence.

- Addiction is considered a health problem. Needle-supply and exchange programmes were introduced to prevent the spread of HIV and AIDs, and methadone is prescribed as a heroin substitute to aid withdrawal.

- Since prevention is the main focus, preventive measures are targeted at young people. Schools provide information on the risks of drugs, alcohol, tobacco and gambling, and emphasise the dangers of driving while under the influence of drugs and alcohol.

- Dutch policy on drugs has given local authorities more power to deal with drug-related disturbances; stepped up co-operation with neighbouring countries to curb drug tourism; allowed tougher action to stop the production and traffic of drugs; and provided more money for specialised care services for addicts.

Drug use Among the Population Aged 12 Years and Over

	Netherlands	United States of America
Cannabis used at least once	15.6%	32.9%
Tried cocaine	2.1%	10.5%
Using heroin occasionally	0.3%	0.9%

Number of "Acute Drug-Related Deaths"

Country	*1994*	*1999*	*'99 per million pop**
Austria	173	128	8.1
Belgium	375	n.a.	n.a.
Denmark	271	239	44.3
France	564	118	2.0
German	1624	1812	22.1
Greece	146	255	24.2
Ireland	19	97	25.7
Italy	867	1002	17.4
Luxemburg	29	18	40.9
The Netherlands	50	76	4.8
Portugal	143	369	36.9
Spain	367	258	6.5
Sweden	85	99	11.2
United Kingdom	2861	3485	58.4

*According to national definitions used to report cases to the EMCDDA

BOB AINSWORTH

PARLIAMENTARY UNDER-SECRETARY AT THE HOME OFFICE RESPONSIBLE FOR DRUG CO-ORDINATION

BACKGROUND TO GOVERNMENT DRUG POLICY

- Before 1998 drug strategy was fragmented around different departments within the government.
- The main increase in the drug problem took place in the late 1980s and early 1990s
- In 1998 it was decided that a strategic overview of drug policy was required in an attempt to marry together the different elements of government activity related to drugs. It was at this time that the drug tsar was appointed.
- Despite frustration among practitioners caused by the absence of pure evidence-based policy formulation, some advance was achieved by focusing on a holistic approach.
- A concerted attempt was made to assimilate law enforcement, treatment, demand, supply, and education strands of government activity in order to point the people dealing with the drug problem in the right direction.
- As a result of the thin evidence base, many of the targets set were unrealistically optimistic.
- Over the last year drug strategy has been reviewed, and a new report is about to be published.
- The aspiration is to improve the co-operation between the Department of Health, Department of Education, and the Home Office. The government is trying to open up space in order to work towards *harm minimization*, focusing on problematic drug users, and targeting effective treatment.

LEADING TO THE PRESENT DAY…..

- The present review has received much media attention, incited much debate and is high on the political scale, but it is not a radical departure from the original approach.
- The growing evidence base should result in more realistic targets and more effective policies.
- Resources need to be re-allocated to reducing demand and finding effective treatments. Evidence suggests that treatment is about three times more effective than criminal justice interventions.
- The drug strategy will remain a holistic approach to the problem.

SPECIFIC CONSIDERATIONS

HEROIN

- The focus must be on *harm minimization* in order to prevent unnecessary deaths, and find appropriate evidence-based prescriptions for opiate users. .
- While heroin prescription should not be the treatment of choice, it should not be dismissed due to political fear and pressure, and lack of confidence by the medical profession.
- The aim is to increase the evidence base and to give the medical profession the guidance and confidence it needs to take the appropriate decisions on what is the appropriate drug for the treatment of the individual heroin addict.
- The Home Secretary has said to the Home Affairs Select Committee that he thought there was more scope for heroin prescription, that it was something that needed to be analyzed, and that these things need to be driven by medical decision and not by political pressure.

STIMULANTS

- Stimulants are a growing problem.
- There is evidence of a move out of amphetamines into cocaine and crack cocaine.
- Crack cocaine is still relatively low-usage by comparison with heroin, but its use is increasing and is associated with far greater levels of violence both by the people who are using it, and by those who are supplying and controlling the trade.
- Less effort has been put into research about crack cocaine, as the problem has not existed for as long, nor is it as widespread as heroin. Thus the evidence base for treatment is very patchy.
- Over the last year expert groups have been formed to draw up appropriate models of care and treatment so that effective practices can be introduced.

CANNABIS

- The main motivation for reclassifying cannabis as a Class C drug was to give consistency and credibility to drug education.
- Because young people have received mixed messages and been given information that is not based on fact and evidence, they do not presently believe what they are told about drugs by the media, their parents, teachers, or politicians.
- The people giving out the information need to be confident in the quality of the education they are providing in order for the message to be heard.
- Treating cannabis as equivalent to hard and lethal drugs like heroin has severely damaged the government's ability to influence public opinion in the drugs arena.
- In order to create a credible and effective educational program, the message must be evidence-based and differentiated with respect to what the different substances do and how harmful they really are.
- The secondary motivation in reclassification was to save police time in dealing with small possessions of cannabis, and thereby allowing the police more time to focus on tackling the supply chain, dealers and hard drugs.

ECSTASY

- The Police Foundation and the Home Affairs Select Committee recommended the reclassification of ecstasy from a Class A to Class B drug.
- Although some of the evidence supports reclassification, it is not felt that the evidence base is strong enough yet.
- It is believed that a lot of harm minimization practices can be introduced without reclassification.
- These include safer clubbing guidance and raising standards in the entertainment venues where ecstasy is widely used by, for example, training staff to recognize signs of distress, installing better ventilation and water fountains.
- The focus will also be on preventing ecstasy entering the premises in the first place.

LAW ENFORCEMENT

- Law enforcement will continue to try to infiltrate the supply chain back to the big suppliers and producer countries, linking up with other jurisdictions in order to do so.
- They will also try to disrupt the trafficking that takes place within this country, and deal with the problems that exist on the streets.
- The Proceeds of Crime Act aims to increase the rate of confiscation of criminal assets by introducing a comprehensive programme of criminal asset recovery. At present the UK confiscates at about a tenth of the rate of Ireland and a quarter of the rate of the US.

SUMMARY

- The aim is to introduce a more comprehensive package of harm minimization: making treatment more effective, putting in more resources, and trying to create the space for evidence-based heroin-prescription by the medical profession.
- The aim is also to become more effective in law enforcement, to dismantle the supply chain and remove the profits, and at the same time try to be more effective on the treatment side, since this is a demand-led business.
- Continue to shift resources towards demand reduction and treatment.
- Improve the quality of education to young people by giving parents and teachers the confidence to speak the truth about substances in a credible and effective way.
- Lift the level of understanding of what these substances do by giving people credible, non-judgmental information so that they can make informed decisions about them.

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APPENDICES

I. BIOGRAPHIES OF SPEAKERS
II. PARTICIPANTS ATTENDING SEMINAR 1
III. THE BECKLEY FOUNDATION

BIOGRAPHIES OF SPEAKERS

COLIN BLAKEMORE
PhD, ScD, FIBiol, FMedSci, FRS
Waynflete Professor of Physiology, University of Oxford
Director of the Oxford Centre for Cognitive Neuroscience

Colin Blakemore studied medical sciences at Cambridge, completed a PhD at the University of California, Berkeley, taught at Cambridge for 11 years, and in 1979 took up the Chair of Physiology at the University of Oxford. He has received many prizes for his research, which has been concerned with vision and the early development of the brain, and he is currently President of the Physiological Society and President of the new Biosciences Federation. He is also passionately committed to the public communication of science and won the Royal Society Michael Faraday Medal in 1989. He has been President and is now Chairman of the British Association for the Advancement of Science. He is a frequent broadcaster on radio (including the BBC Reith Lectures) and television (including the Royal Institution Christmas lectures and *The Mind Machine*, a 13-part series on brain and mind). He has also written widely for the general public: his most recent book is *The Oxford Companion to the Body.* He has contributed to the national debate on drugs, arguing that assessment of harm should be soundly based on scientific evidence, and that we must contemplate more radical approaches to the problem.

T.W. ROBBINS
Department of Experimental Psychology, University of Cambridge

Trevor Robbins gained his first degree and PhD in Psychology from the University of Cambridge, the latter under the supervision of Dr Susan Iversen in Psychopharmacology. He was appointed initially to the faculty in 1973 at the University and gained tenure as a lecturer in 1978. He was appointed first as Reader in Cognitive Neuroscience (1992) and in 1997 as Professor of Cognitive Neuroscience. Recently, he has been elected to the Chair of Experimental Psychology (and HoD) at Cambridge from October 2002. He is a Fellow of the British Psychological Society (BPS) and the Academy of Medical Sciences. In 1982, he won the BPS Spearman Medal for outstanding research. In 1996 he shared the award of the DG Marquis medal for the best paper published that year in the APA journal *Behavioral Neuroscience*. In 1998 he delivered a Hebb Lecture to McGill University and the closing Plenary at FENS in Paris 2002. He has been President of the European Behavioural Pharmacology Society (1992-1994) and he won that Society's inaugural Distinguished Scientist Award in 2001. He was also President of the British Association of Psychopharmacology from 1996 to 1997. He has edited the journal *Psychopharmacology* since 1980 and until recently was Associate Editor of *Behavioral Neuroscience*. He has been a member of Medical Research Council (UK) and chaired the Neuroscience and Mental Health Board until 1999. He was included on a list of the 100 most cited neuroscientists by ISI. He has published over three hundred and fifty full papers and co-edited three books (*Psychology for Medicine: The Prefrontal Cortex*; *Executive and Cognitive Function, and Disorders of Brain and Mind).*

LESLIE IVERSEN
Department of Pharmacology, University of Oxford

Leslie Iversen PhD is Director of the Wolfson Centre for Research on Age Related diseases at Kings College London, Visiting Professor at the Department of Pharmacology, University of Oxford, and founder of the pharmaceutical company Panos Therapeutics Ltd. He was previously Director of the Neuroscience Research Centre set up by the international pharmaceutical company Merck & Co. Inc. in Harlow, Essex, UK (1983-1995) and Director of the UK Medical Research Council Neurochemical Pharmacology Unit in Cambridge, England (1970-1983). He is interested in understanding how drugs work in the nervous system and in the molecular basis of nervous system disorders and is particularly known for his work on the chemical messengers used for communication between nerve cells. He is the author of several books and of more than 350 scientific publications and is a Fellow of the Royal Society of London and a Foreign Associate of the National Academy of Sciences, USA. He acted as the specialist adviser to the House of Lords Science & Technology Committee's enquiry into Cannabis, and his most recent books are "The Science of Marijuana", Oxford University Press, 2000 and "A Very Short Introduction to Drugs", Oxford University Press, 2001.

BARRY J. EVERITT
Department of Experimental Psychology, University of Cambridge

Barry Everitt has a B.Sc. in Zoology and a Ph.D. in Behavioural Neuroendocrinology from the University of Birmingham Medical School in 1970. Following a postdoctoral position in neuroscience at the Karolinska Institute, he joined the Department of Anatomy at the University of Cambridge as a lecturer, then Reader in Neuroscience. In 1995, he moved to the Department of Experimental Psychology in Cambridge and was appointed to a personal Professorship in Behavioural Neuroscience in 1997. He has been President of the British Association for Psychopharmacology, President of the European Brain and Behaviour Society and is president-elect of the European Behavioural Pharmacology Society. He is also Editor-in-Chief of the European Journal of Neuroscience. His major research interests at present concern the neural and psychological basis of cocaine and heroin addiction, especially the importance of interactions between these drugs and learning systems in the brain which result in drug-seeking and drug-taking becoming compulsive habits. A key aspect of his research concerns the development of novel treatments for addiction based on preventing relapse when individuals are exposed to drug cues that induce craving.

DAVID J. NUTT
DM, FRCP, FRCPsych, FMedSci
Department of Clinical Medicine, University of Bristol

David Nutt is currently Professor of Psychopharmacology, Head of the Department of Clinical Medicine and Dean of Clinical Medicine and Dentistry, based at the University of Bristol. He received his undergraduate training in medicine at Cambridge and Guy's Hospital, and continued training in neurology to MRCP. After completing his psychiatric training in Oxford, he continued there as a lecturer and then later as a Wellcome Senior Fellow in psychiatry. He then spent two years as Chief of the Section of Clinical Science in the National Institute of Alcohol Abuse and Alcoholism in NIH, Bethesda, USA. On returning to England in 1988 he set up the Psychopharmacology Unit in Bristol, an interdisciplinary research grouping spanning the departments of Psychiatry and Pharmacology. He is currently a member of the Advisory Council on the Misuse of Drugs, and Chair of the Technical Committee of the ACMD, the Committee on Safety of Medicines. In addition, he is advisor to the British National Formulary, the editor of the Journal of Psychopharmacology and the Past-President of the British Association of Psychopharmacology.

MARK A. GEYER
Department of Psychiatry, University of California, San Diego

Dr. Geyer is a preclinical psychopharmacologist at the University of California, San Diego, where he currently holds the position of Professor of Psychiatry and Neurosciences in the School of Medicine. He is actively involved in both the Ph.D. Group in Neurosciences and the Clinical Psychology Ph.D. Program. Since receiving his doctorate in Psychology in 1972, he has focused on basic research addressing the behavioral and neurobiological effects of drugs acting via monoaminergic neurotransmitters. For over two decades, he has had continuous funding from the U.S. National Institute on Drug Abuse to study the behavioral effects of hallucinogens in animals. Dr. Geyer is also internationally known for his research on the psychophysiology, neurobiology, and pharmacotherapy of schizophrenia, which is supported by multiple grants from the National Institute of Mental Health. He has published over 250 peer-reviewed papers, including many addressing the mechanisms subserving the effects of psychostimulants, hallucinogens, and entactogens. Dr. Geyer is currently an editor for two highly-respected international journals, *Psychopharmacology* and *Neuropharmacology*, and is on the Editorial Board of several other journals. Dr. Geyer was one of the co-founders of the Heffter Research Institute, which reviews and funds rigorous research on psychedelic compounds and publishes the Heffter Review. He is currently the President of the International Behavioral Neuroscience Society, Vice-President of the international Serotonin Club, and a member of the Scientific Council of NARSAD.

MICHAEL FARRELL
Consultant Psychiatrist, National Addiction Centre

Dr Michael Farrell, is a Senior Lecturer and Consultant Psychiatrist at the National Addiction Centre and Maudsley Hospital London. He is responsible for a large community based drug and alcohol service in South London. He is involved in research and policy aspects of drug and alcohol problems. He has conducted research on the relationship between drug, alcohol, tobacco use and other forms of psychiatric morbidity. He has conducted a range of treatment evaluation projects. He has worked in partnership with the Office in National Statistics on the programme of surveys of psychiatric morbidity which has included two national household surveys, a prisons survey, a homeless survey and a survey of child and adolescent mental health. He has worked part time as a policy advisor to the Department of Health. He is an editor with the Cochrane Collaboration Alcohol and Drugs Group involved in the review of effective interventions for drug and alcohol dependence. He has worked with a wide range of international organisations and is also a member of the WHO Expert Committee on Drug Dependence. He has published over 200 articles on aspects of tobacco, alcohol and drug use and dependence.

PARTICIPANTS WHO ATTENDED SEMINAR 1

Bob Ainsworth MP	*Parliamentary Under-Secretary of State for Anti-Drugs Co-ordination and Organised Crime*
Nick Barton	*Chief Executive, Clouds House*
Prof. Colin Blakemore	*Waynflete Professor of Physiology, University of Oxford*
Richard Brunstron	*Chief Constable of North Wales*
Yolande Burgin	*Director, The Independent Inquiry into Drug Testing at Work*
Eric Carlin	*Chief Executive of Mentor Foundation*
Dr. Mark Collins	*Associate Medical Director, The Priory, Roehampton*
Rod Dalley	*Vice Chairman Elect, Police Federation of England and Wales*
Richard Davenport-Hines	*Author 'The Pursuit of Oblivion, A Global History of Narcotics'*
Dr. Pat di Ciano	*Dept. of Psychology, University of Cambridge. Raconteur.*
Prof. Barry Everitt	*Professor of Behavioural Neuroscience, University of Cambridge*
Dr. Michael Farrell	*Consultant Psychiatrist, National Addiction Centre*
Prof. Cindy Fazey	*Professor of International Drug Policy, University of Liverpool*
Prof. Mark Geyer	*Professor of Psychiatry and Neurosciences, University of California*
Tony Gilland	*Director of Science and Society, Institute of Ideas*
Fulton Gillespie	*Parent*
Tony Hall	*Head of Drugs Legislation Section, Drugs Strategy Directorate, Home Office*
Paul Hayes	*Chief Executive, National Treatment Agency for Substance Misuse*
Roger Howard	*Chief Executive of Drugscope*
Prof. Leslie Iversen	*Professor of Pharmacology. University of Oxford. Author of 'The Science of Marijuana'*
Mike Jay	*Historian and Author*
Charlie Lloyd	*Joseph Rowntree Foundation*
Dr. José-Ramon Lopez-Portillo	*Former Chairman of the Council of the F.A.O. United Nations*

Dr. Athina Markou	*Department of Neuropharmacology, The Scripps Research Institute*
Dr. John Marks	*Ran the Chapel Street Clinic, Liverpool*
Tristan Millington-Drake	*Chief Executive, The Chemical Dependency Centre*
Sir Keith Morris	*Former Ambassador of Columbia*
Amanda, Lady Neidpath	*Director, The Beckley Foundation*
Bill Nelles	*General Secretary, The Methadone Alliance*
Prof. David Nutt	*Professor of Psychopharmacology and Head of Department of Clinical Medicine, University of Bristol*
Brian Paddick	*Commander, Metropolitan Police*
Dr. Mark Peplow	*Science Information Officer, The Royal Institution*
Fredrick Polak MD	*Consultant Psychiatrist, Member of the Board of the Netherlands Drug Policy Foundation*
Fabrice Pothier	*Representative from NEF-EDPF*
Dr. Alex Richardson	*Senior Research Fellow, Physiology Department, Oxford*
Prof. Trevor Robbins	*Professor of Cognitive Neuroscience, University of Cambridge*
Ian Robinson	*Chief Executive of the E.A.T.A. (the European Association for the Treatment of Addiction)*
Dr. Phillip Robson	*Senior Research Fellow, Department of Psychiatry Oxford, Medical Director of G.W. Pharma*
Prof. John Stein	*Professor of Neurophysiology, Magdalen College Oxford*
Prof. Dai Stephens	*Professor Experimental Psychology, University of Sussex*
Charles Tallack	*Performance and Innovation Unit, Cabinet Office*
Mike Trace	*National Treatment Agency, and Chairman of European Monitoring Centre for Drugs and Drug Addiction, Lisbon*
Jan Wiarda	*Chief of Police, The Hague*
Sir Richard Wilson	*Master of Emmanuel College, Cambridge. Former Secretary of the Cabinet and Head of the Home Civil Service*

THE BECKLEY FOUNDATION

The Beckley Foundation is a charitable trust set up to promote the investigation of consciousness from the perspectives of science, health, politics and history. Its activities include supporting and directing research programs, seminars and conferences to inform researchers, professionals and the public.

It has a particular interest in the comparative study of changes in consciousness brought about by such diverse activities as the practice of yoga, meditation and some forms of exercise and nutrition, as well as the use of legal and illicit drugs.

- The Foundation's main scientific objective is to research the neurophysiology underlying changes in consciousness, especially those associated with heightened creativity, elevated awareness and positive mood.

- The Foundation's social objective is to promote public health by supporting world-class scientific research into consciousness and its modulation from a multi-disciplinary perspective; and by disseminating the information to academics, policy-makers and the public.

The Beckley Foundation particularly seeks to promote the understanding of how this knowledge may be used to enhance health, ameliorate mental and physical illness, and comfort the dying. It also aims to investigate how best to encourage the avoidance of those practices that lead to poor health and addiction.

A key aspect of the Foundation's activities is to support and organise seminars and conferences where leading experts from a wide range of disciplines can analyse and explore the social and health implications of the latest scientific knowledge. This seminar on 'Drugs and the Brain', held at Magdalen College, Oxford on 22 Oct 2002, is the first in the series entitled 'Society and Drugs: A Rational Perspective'.

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