

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.