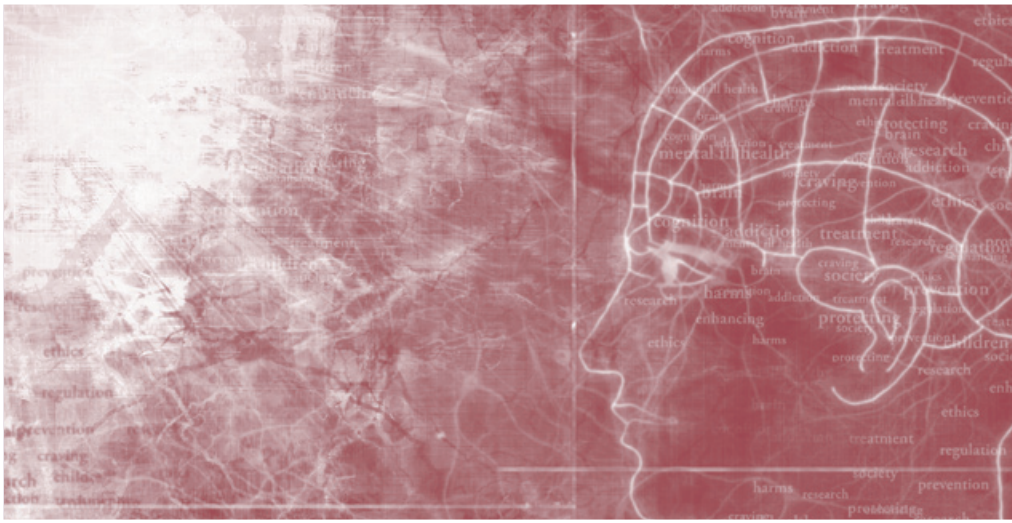
The Academy of Medical Sciences



Brain science, addiction and drugs

Report Synopsis

May 2008

The Academy of Medical Sciences

The Academy of Medical Sciences promotes advances in medical science and campaigns to ensure these are converted into healthcare benefits for society. Our Fellows are the UK's leading medical scientists from hospitals and general practice, academia, industry and the public service.
The Academy plays a pivotal role in determining the future of medical science in the UK, and the benefits that society will enjoy in years to come. We champion the UK's strengths in medical science, including the unique opportunities for research afforded by the NHS, encourage the implementation of new ideas and solutions – often through novel partnerships, promote careers and capacity building and help to remove barriers to progress.

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Introduction

In July 2005 the Government initiated a Foresight project to consider how we can manage the future use of psychoactive substances to best advantage for the individual, the community and society. The psychoactive drugs considered were so-called 'recreational' drugs, medicines for mental health and a new type of drug called a 'cognition enhancer', which can affect brain performance in specific ways. The Foresight project culminated in the publication of a report 'Drugs Futures 2025?', following which the Academy of Medical Sciences was asked by the Department of Health 'to consider the societal, health, safety and environmental issues raised in the Foresight project and to formulate recommendations for future research needs and public policy'.

In early 2006, the Academy convened a working group of Fellows and outside experts, chaired by Professor Sir Gabriel Horn FRS FRCP, to undertake this task. To take account of a wider range of voices than are normally heard in such projects, the Academy also commissioned a nationwide programme of public engagement activities. The final report was shaped not only by the analysis and discussions of the working group, but also by the views that emerged during the public engagement events. This report synopsis is intended for non-specialists and lay readers; the full report, and further details on the project, can be found at http://www.acmedsci.ac.uk.

Brain science, addiction and drugs: a better understanding

Every organ in the body is susceptible to the action of some or many types of drug. This report focuses on those that affect the workings of the brain: in the jargon of the trade, psychoactive drugs.

In the twelve decades since the discovery that the individual unit of structure and function within the nervous system is the nerve cell or neuron, science has developed a broad understanding of the way in which our brains sense the world, think about it, and act on it. The brain itself comprises some 10-11 billion nerve cells. These are in continual communication via specialised junctions or synapses, which allow adjacent nerve cells to form inter-connected circuits. The signal or message that crosses the gap between adjacent cells is a tiny amount of a collection of chemical substances known as neurotransmitters. Produced on one side of the gap these modify activity in a neighbouring neuron by interacting with specialised surface sites called receptors. The vast number of these synapses, these interconnections – far more than in any manmade computer – is what gives the human brain its unique power and flexibility.

Whether taken medicinally or for recreation, many psychoactive drugs work by interfering with these interconnections. Some amplify transmission; others shut it down. Some drugs, especially those with the potential for causing addiction, subvert the circuitry so completely that they have profound or distorting effects on its normal working.

Environmental factors ranging from where you live to whom you mix with have long been known to influence your likelihood of becoming addicted to a drug, irrespective of its legality. It is now clear that genetics can influence the risk too. You may inherit a gene or genes that, for example, make the system more responsive to certain drugs: so that they give you a bigger, more seductive 'high'.

In spite of such advances, our grasp of the detailed workings of the brain is far from complete. In due course we will no doubt learn much more. This

understanding will aid the development of better drugs for healing brain and psychiatric disorders, and for handling addiction. But science cannot by itself answer ethical and social questions about psychoactive drugs. Should we use pharmacology to alter our minds or to improve them? Is it, on balance, desirable? And who should decide?

How big a problem is drug abuse?

Big, certainly. The UK Government spends more than £15 billion annually in meeting the cost of drug-related social and economic harms. Estimates for England and Wales suggest that more than 11 million people aged 16-59 have used illicit drugs during their lifetime. In the UK as a whole, young people are thought to be among the heaviest licit and illicit drug users in Europe. But not all the published figures are reliable, and this makes it difficult to be certain about trends.

Having a single organisation to work with academics in reviewing the data would make it easier to monitor how changes in policy impact on trends in drug use. So would the development of what are called 'evidence synthesis methods', by which data from many sources are combined to improve the reliability of statistics.

Understanding addiction

Through advances in brain science over the past 30 years, researchers can now identify the primary sites of action of many psychoactive drugs. This has revealed that many act on receptors in a region of the brain known as the nucleus accumbens. Moreover, the parts of the brain involved in drug addiction also feature in behavioural addictions such as gambling and over-eating. This realisation, supported by animal as well as human studies, has generated several plausible theories of addiction. Several of these theories emphasise the role of the nucleus accumbens as a point of contact between parts of the brain concerned with motivation and reward, and parts that influence behaviour. It may be that psychoactive drugs, having in effect hijacked this point of contact,

reward (and so reinforce) unhelpful or self-destructive behaviours. Addicts come to prefer small immediate rewards to potentially larger but delayed ones. Addiction, in medical terms, can be described as a 'chronic relapsing brain disorder'.

Sadly, these insights have so far had little impact on the discovery of new medicines for addiction. Most existing medicines aim for the modest goal of harm reduction: the replacement of an addictive drug with something possibly less addictive and certainly less hazardous. Hence the use of methadone for heroin addicts, and nicotine patches for smokers.

Vaccines to recognise and neutralise psychoactive drugs are being trialled to reduce dependence on smoking cigarettes. However the practical and ethical hurdles that would have to be overcome in using vaccines more widely are considerable.

Recent insights into the molecular mechanisms of addiction should lead to the development of new drugs targeted at the receptors involved, but only if there is additional investment to ensure this knowledge is translated into practical benefits for patients and addicts. There are several vital research topics that should be prioritised. These range from the molecular changes that occur during addiction, to the means by which genes and environment influence the propensity to abuse drugs. Improved co-ordination among researchers across Europe would make it easier to study some of these issues.

What to do about addiction?

The stated aim of the UK Government's policy on drug abuse is 'to reduce the harm that drugs cause to society'. Views on what this means for practical policy vary depending on how ideas of 'freedom of choice' are balanced against a need to regulate or prohibit certain activities.

Feedback from the public engagement work supported the view that, in a liberal democracy, the intelligent and appropriate regulation of recreational

drugs presupposes a prior and widespread public debate. Policies will be philosophically and legally sound only if based on the best available information about the harms that different drugs actually cause. We therefore emphasise that the framework of classification, the place of each drug in that framework, and the sanctions imposed on drug users, should all be based on evidence of the harms associated with individual drugs. Our report puts forward an outline of an evidence-based scheme for comparing the damage done by different drugs: physical harms (acute and chronic); social harms; and harms to mental health. The report also stresses that, in developing effective policy measures, the aim of Government should be to strike a balance between individual freedom and the harms caused to individuals, families and society.

Addiction, ideally, should be prevented; but to achieve this aim we need to understand why people become addicted in the first place. Factors known or suspected to put people at risk include: personality characteristics such as impulsiveness; genetic factors; neglect, abuse and similar family pressures; community influences such as the availability of drugs and the attitudes of peer groups; and the media. Other biological and social influences may act protectively.

Although we still need a better understanding of how these influences bear on individuals, action cannot be delayed. So any intervention now planned should be evaluated through controlled trials and long term follow-up.

Medicines for mental health

Roughly one in ten of the world's population suffers from a mental illness. In England alone these conditions cost the community around £77 billion annually. To say that effective medicines are essential is to state the obvious.

Brain science has already brought profound changes to psychiatry. Many mental illnesses can be described as failures of information processing by inter-connected systems within the brain. Such insights should, eventually, offer new treatments.

In the meantime it may surprise people to learn that the effectiveness even of current treatments compares favourably with that of drugs used elsewhere in medicine. And psychiatric treatment can transform lives. However, today's drugs have their limitations. Some are only partially effective; not all patients respond to them; and some drugs, through adverse effects ranging from weight gain to nausea, are poorly tolerated.

The promise of brain science is the development of new, effective treatments that have minimal side effects. In some cases the first steps have already been taken. The role of inherited susceptibility in conditions such as schizophrenia and bipolar disorder is increasingly well understood. Many genes that are possibly involved have been identified; some are being studied. Reassurance that research is on the right lines comes from knowing that some of these genes code for the production of neurotransmitters which operate at the sites of action of drugs currently used in psychiatry.

Future possibilities are exciting and numerous. To take one example, some genes are thought to make the brain vulnerable to mental illness by altering the development of its wiring. Any such mis-wiring would be difficult to overcome. However, a brief pulse of drug treatment at a critical moment might prevent a particular gene inflicting its damaging effect on the brain. Equally intriguing is the likelihood that understanding the genetic basis of mental illnesses will alter their classification and diagnosis – with consequent effects on how they are treated.

There is no lack of potential targets at which the pharmaceutical industry can direct new drugs. The challenge lies in identifying the best of them at the earliest opportunity.

If the promise of brain science is new treatments, the claim of brain science is that these goals are attainable – so long as we are prepared to invest in the necessary research.

Drugs to enhance us

Cognition enhancers – drugs to boost brain activities such as attention, memory, language, planning and decision-making – are one of pharmacology's more recent achievements. Used medically to treat patients suffering from dementia, stroke, and other neurological disorders, they also offer the possibility of benefit to healthy individuals.

Twenty seven such agents were identified in the Foresight report, 'Drugs Futures 2025?'. Ten are dietary supplements; most of the rest are pharmaceutical drugs that work by enhancing (or diminishing) transmission across certain synapses. A number of these drugs produce a modest level of cognitive enhancement in, for example, patients with Alzheimer's disease. But the evidence is still relatively limited; and for dietary supplements there is even less.

The evidence of benefit in healthy users is slimmer still, and there are no major research programmes devoted to this application. But the availability of drugs bought via the internet already encourages the curious and the hopeful to try their luck.

The relationship between the performance of synapses, the use of drugs to boost their activity, and any resulting cognitive benefit remains uncertain. Doses of otherwise effective drugs which are too high as well as too low may both lead to a drop-off in synapse performance, and so also in cognition. Moreover there may be different optimum doses for different functions; it may not be possible to maximise performance in all types of brain function at the same time.

In spite of these difficulties, our grasp of the molecular events underpinning learning and memory do suggest that cognitive enhancement should be taken seriously by bodies such as the Food Standards Agency and the Medicines and Health Care Regulatory Authority. Regulators might well need to consider

whether the competitive use of cognitive enhancers (as in cramming for an exam) should be viewed in the same light as their non-competitive use - say for minimising everyday matters such as forgetfulness.

What does the public think about all this?

While no two people hold identical views on issues as multi-layered as the use and abuse of psychoactive drugs, the public consultation did reveal common ground. The value of using them to improve mental health was widely endorsed - though with reservations if drug therapy was a 'quick fix' alternative to longer-lasting solutions, or used solely to control behaviour deviating from certain norms. There was a strong feeling that drugs should be used in conjunction with non-pharmacological treatments, not as an alternative to them.

The development of cognition enhancing drugs to delay or halt dementia was also applauded by participants. But there was less certainty about their use in healthy people – for whom drug enhancement was seen to be 'unnatural' and less desirable as a stimulant to brain power than a good diet and plenty of exercise. People also expressed fears about the adverse effects of such drugs, equality of access to them, undue pressure to use them, and their possible effect in devaluing unaided achievement.

Many spoke of the pleasurable effects of recreational drugs, and suggested that the desire to change one’s state of mind is part of human nature. Some owned up to the excitement of acting illegally. Others were more concerned about the harm caused by drugs, legal and illegal. There was a widely held view that current drug classification is 'confused, inconsistent and arbitrary' and needs rethinking.

There was also support for the individual right - subject to age, and supported by education - to make one’s own choices, irrespective of the type of drug use in question.

The most strongly felt hopes and concerns can be captured by describing two possible futures. Among the items listed in a negative view of the future were:

- Mental illness and addiction becoming more stigmatised and less visible.
- An increased use of licit and illicit recreational drugs.
- The use of cognition enhancers driven by social pressure.
- The use of drugs to control rather than treat older people and the mentally ill.

A more positive future might include:

- The development of new therapeutic drugs for mental illness with minimal side effects.
- Less punitive and more knowledgeable therapeutic attitudes to drug abuse.
- More drugs education for children.

The outcomes of the public engagement events provide evidence of people's capacity to grapple with the scientific and policy issues raised by drugs, addiction and mental health. The development of future policies should be guided by the principle of openness, and not settled without prior public discussion.

Five key messages

1. Brain science offers the promise of better treatments for mental illness and addiction, but not without further investment.
2. The formulation of better strategies for preventing mental illness and drug abuse will require a deeper understanding of the factors that put people at risk.
3. There is a need for better information on the prevalence and use of all types of recreational drug.
4. The regulation of recreational drug use requires a more sophisticated index of their various harms.
5. Policy on all forms of psychoactive drug use must be informed by research findings and by the views of the public.

To understand how the brain works was one of the key challenges of the 20th century. The challenge for the 21st century is to deepen that understanding, and to use it for the benefit of society.

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