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If one believes that the brain is, in some as yet unspecified way, the organ of mind and behaviour, then all human behaviour has a neurobiological basis. Neuroscience research over the past several decades has provided more specific reasons for believing that many addictive phenomena have a neurobiological basis. The major psychoactive drugs of dependence have been shown to act on neurotransmitter systems in the brain (Nutt 1997; Koob 2000); common neurochemical mechanisms underlie many of the rewarding effects of these drugs and the phenomena of tolerance and withdrawal symptoms (Hyman & Malenka 2001; Koob 2000), and there is evidence for a genetic vulnerability to addiction (Nestler 2001; Uhl 1999) that is mediated by genes that regulate the metabolism of psychoactive drugs and the brain neurotransmitter systems on which they act (Uhl 1999).

Neuroscience research on addiction has the potential to improve treatment of drug dependence (Nutt 1997). It may lead to more effective ways of helping drug-dependent people to withdraw from their drug of dependence and it may increase their chances of remaining abstinent (Koob 2000). We may also have immunological prostheses for relapse prevention—'drug vaccines'—that help former addicts remain abstinent by preventing their drug of choice from acting on receptors in their brains during the period when they are most vulnerable to relapse (Fox 1997; Hall 2002). Genotyping of people seeking help to deal with addiction may enable patients to be better matched to pharmacological treatments, e.g. by predicting whether smokers were more likely to quit with bupropion or nicotine replacement (Munafo *et al* . 2001; Walton *et al* . 2001).

Neuroscience perspectives on addiction have more mixed social implications for 'governing images' of addiction. According to one influential interpreter of neuroscience research, addiction is a 'chronic, relapsing brain disease' (Leshner 1997), a disorder in which chronic drug use flicks a metaphorical switch in the brain after which the person's drug use is beyond their control (Leshner 1997). This view challenges the common-sense view of addiction as a matter of individual choice that can be influenced by threats of punishment and imprisonment.

A neurochemical basis for addiction makes possible a more humane, less punitive response to addiction. It raises the prospect of increased funding for addiction treatment, less resort to imprisonment as the first-line treatment for addiction and less stigmatization of those who are addicted to drugs. It is, for these reasons, a view that appeals to some people who are addicted to drugs and to some of their families. Addiction as a 'brain disease' has some of the appeal of the older 'disease models' of addiction, with the added authority of the latest science. A 'disease' that can be 'seen' in the many-hued splendour of a PET scan carries more conviction than one justified by the possibly exculpatory self-reports of addicts who claim that they are unable to control their drug use.

The depiction of addiction as a brain disease has benefited addiction research in the competition for funding with neuroscientists working on disorders such as dementia, bipolar disorder and schizophrenia. Increased funding for neuroscience research has meant that some addiction researchers have been the beneficiaries of the view that addiction is a brain disease, a view about which other addiction researchers have been more sceptical, if publicly silent about the reasons for their scepticism. A reviewer of this editorial described the thesis that addiction is a chronic brain disease as a Faustian bargain that secured increased research funding but with costs that are only now becoming apparent.

Simplified versions of neuroscience views of addiction depict addicts' behaviour as being controlled by the state of their brain

receptors and neurotransmitter systems. This view seems to warrant heroic treatment interventions, such as ultra-rapid opiate detoxification for heroin dependence, encouraging impoverished patients and their families to pay the substantial sums charged for these treatments by some entrepreneurs (Hall 2000). A chronic relapsing brain disease may also be seen as authorizing legally coerced treatment because drugdependent people are incapable of acting in their own best interests.

Another possible disadvantage of a neuroscience-based disease model of addiction is now emerging. Bioethicists in the United States have argued recently that addicts lack the capacity to give free and informed consent to participate in: (1) experimental neurobiological studies of addiction (e.g. using PET scans) that involve giving drugs of dependence to addicts (Cohen 2002); and (2) clinical trials of injectable heroin as a treatment for opioid dependence (Charland 2002). The requirement that research participants provide free and informed consent has been an ethical *sine qua non* of biomedical

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research since the Nuremberg Code (Brody 1998). Hence, if these bioethicists' arguments are accepted by ethical review committees, they will severely constrain the type of research that it is ethical to conduct in the country that funds most of the world's research on addiction. Until now, the view among addiction researchers has been that drug-dependent people are able to give free and informed consent to participate in research studies and clinical trials so long as they are not intoxicated or suffering acute withdrawal symptoms at the time that they give consent (e.g. College on Problems of Drug Dependence 1995; Gorelick *et al* . 1998). This view has been called into question by Charland (2002) and Cohen (2002), who have taken the defining characteristics of drug dependence in DSM-IV—especially the loss of control over drug use—to mean that people who are drug dependent lack the capacity to give free and informed consent to participate in research studies in which they may be given their drug of dependence.

Cohen (2002) argues that 'the nature and pathology of untreated substance dependence make the condition inherently incompatible with a rational, internally uncoerced and informed consent on the part of those volunteering to receive addictive drugs in a non-therapeutic research setting' (p. 74). This 'may no longer obtain', he argues, after addicts have undergone treatment. According to Cohen, it is only ethical to give drugs of dependence in experimental studies to abstinent addicts and, possibly, those who are already in treatment.

Even though research suggests that alcohol and drug-dependent people who participate in research are helped rather than harmed (e.g. Dolinsky & Babor 1997; Gorelick *et al* . 1998), we anticipate a lack of enthusiasm among members of ethics committees for allowing studies that administer drugs of dependence to abstinent addicts. We think it is more likely that ethics committees will accept the first of Cohen's arguments and reject the second. If so, the outcome will be that no experimental research will be permitted in which drug-dependent people receive their drug of dependence.

Charland (2002) has used a similar argument to arrive at the conclusion that heroin addicts are unable to give free and informed consent to participate in heroin prescription trials. Heroin addicts, he argues on the testimony of one former heroin addict, are incapable of saying 'no' to the offer of free heroin because of their addiction. Untreated heroin addicts offered their drug of dependence are 'vulnerable subjects' in the terminology of the US National Bioethics Advisory Committee (1998), which means that they cannot serve as experimental subjects in such studies, or they can do so only if consent is given on their behalf by others. If taken seriously these views would prevent addicts from participating in clinical research from which they stand to benefit. Even if not fully accepted, such arguments may reduce the preparedness of ethics committees to allow clinical and experimental research on addiction that involves the use of drugs of dependence.

Charland argues that the only free and informed decision that an addict is capable of making is to enter abstinence- orientated treatment. However, using Charland's reasoning, even this decision may not be truly free or informed. Many addicts enter abstinent-orientated treatment under some form of coercion, either the threat of criminal prosecution or the loss of employment or a relationship. Heroin addicts who enter such treatment may overestimate their capacity to achieve abstinence, underestimate the difficulties of remaining abstinent, and may not appreciate the risks of attempting abstinence (e.g. of fatal overdose on relapse to heroin use). If the standards for free and informed consent are set high enough, no one will meet them. Most people who become parents, for example, would probably concede in retrospect that this was not a decision to which they gave informed consent. We do not use this fact, however, to prevent people from reproducing. Partially informed decisions, misplaced confidence and decisional regret are an integral part of the human condition.

Charland's claim that heroin users are unable to say 'no' to an offer of heroin is also empirically false because the Swiss heroin trials were not inundated with untreated heroin addicts demanding 'free heroin'. This is clear in the report of a randomized controlled trial of immediate versus delayed entry to heroin maintenance (with the delayed entry group given access to usual treatment, methadone maintenance or abstinence) (Perneger *et al* . 1998). The researchers intended to recruit 40 patients in each group but recruited only 24 and 27 patients, respectively. Moreover, when offered the choice at the end of 6 months, two-thirds of those in the delayed entry to heroin treatment group decided against receiving heroin (Perneger *et al* . 1998). Severely dependent treatment refractory Swiss heroin addicts were thus capable of saying 'no' to an offer of heroin prescription.

Charland does not place heroin maintenance within a realistic set of alternatives for heroin addicts who have failed repeatedly at treatment, in whom the chances of achieving enduring abstinence are very low. Instead, he assumes unrealistically that most heroin users seeking some form of heroin maintenance treatment have a high chance of achieving abstinence in abstinence-orientated treatment programmes. He assumes implicitly that entry to heroin maintenance treatment reduces the chances of achieving abstinence. Both assumptions are probably wrong. Longitudinal studies of heroin-dependent people show that annual rates of achieving enduring abstinence are not very different from the annual mortality rate

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(Gerstein & Harwood 1990, ch. 4; Hser *et al* . 1993; Goldstein & Herrera 1995). Moreover, rates of abstinence 5 years after treatment entry are the same in people who enter drug-free treatment as in those who enter methadone maintenance (Maddux & Desmond 1992).

CONCLUSIONS

Neuroscience models have much to offer the field of addiction, but they will be self-defeating if they lead to severe restrictions on the type of neuroscience research that can conducted in future. A major challenge for the addiction field is to integrate the insights that neuroscience research has provided on drug use and addiction with those provided about drug use and addiction by clinical, epidemiological, sociological and economic research. The challenge is (1) to develop theories of addiction that take seriously the neurobiological bases for drug effects and addictive phenomena; (2) without depicting addicts as automatons whose behaviour is under the control of the drugs acting on the receptors sites in their brains; and (3) while recognizing the opportunities for individual decision, interpersonal influence and social policy to affect the drug use and the behaviour of drug-dependent people.

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