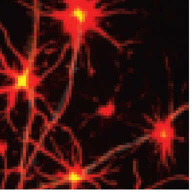

Neuroimaging – summary

Our knowledge of how drugs affect the brain is being improved by our ability to image the brain and brain processes. Imaging methods now in use or on the horizon may allow us to view the brain circuits involved in addiction and form a better understanding of aspects of addiction such as craving and relapse.

The Foresight project on Brain Science, Addiction and Drugs asked Hugh Garavan of Trinity College Dublin, Anne Lingford-Hughes of the University of Bristol, Terry Jones of the University of Manchester, Peter Morris of the University of Nottingham, John Rothwell of University College London and Steve Williams of the Institute of Psychiatry, King's College London, to look at the potential for imaging to inform our knowledge of addiction and drug use.

What can imaging do?

Today's imaging techniques allow the neural circuits involved in addiction to be identified and researched. Scanning methods including positron emission tomography (PET) and single photon emission tomography (SPET) allow us to measure changes in blood flow, metabolism and chemicals in the brain. These methods have been supplemented by functional magnetic resonance imaging (fMRI) which measures blood flow. FMRI gives us a greater ability to measure changes in activity occurring in seconds. Our ability to resolve processes occurring in smaller brain areas and observe them over time is growing. And advances in technology mean that it is becoming increasingly feasible to image animal as well as human brains.

PET and SPET have allowed the chemical effects of addiction to be characterised in the dopamine system, which is known to be a key brain system associated with addiction and reward. Imaging allows the lower levels of dopamine receptors associated with addiction to be observed directly, as can the increased levels of the neurotransmitter dopamine associated with drug use.

Most such work has been carried out with cocaine addiction and has shown that the neural basis for the increased propensity to addiction are influenced by environmental factors such as social hierarchy. Differences in brain chemistry between people who are susceptible to different forms of alcoholism are also becoming apparent.

Work on opioid dependency has used imaging technology to show the increased level of opioid receptors in the brains of people susceptible to this addiction, and the blocking effect of opioid antagonists.

The use of small-animal scanners is in its infancy but fMRI has been used to demonstrate that tolerance of nicotine and of opiates is associated with specific brain areas in the rat.

Craving

As well as the drug effects themselves, modelling can view the neural effects of drug expectations, such as the craving for drugs and the effects of drug cues. These include increased activity in parts of the brain associated with emotional control, attention and planning. Activation in the same brain areas has been obtained consistently for several drugs of abuse.

Decision making

Addiction involves impaired decision making. An addict is willing to compromise their future well-being for an immediate reward. Imaging of people performing a standard psychological test has shown that brain regions called the anterior cingulate cortex and the ventral prefrontal cortex perform at a low level in addicts. These areas are associated with decision making.

This result is consistent across a range of abused drugs and shows the neural basis for susceptibility to addiction. Work with cocaine also shows that its use can enhance such brain functions, including those damaged by drug use and those whose initial low level of activity may have been associated with a propensity to use drugs.

Future technology

PET is a powerful technology, particularly for exploring the neurochemistry of addiction. New markers and probes will allow receptors and pathways to be mapped in detail. This will require the participation of the pharmaceutical industry. The authors call for new centres for medical and research imaging, where the best technology and methodology would be applied and high standards of research ethics ensured.

In fMRI, progress could be made from *more powerful* machines with a field of 3 Tesla up to perhaps 7 Tesla (about 150,000 times the strength of the Earth's magnetic field). This would allow smaller brain areas to be resolved and single brain events to be imaged in one experiment. With less powerful machines, it is necessary to add together many images. More powerful machines would also allow magnetic resonance spectroscopy methods to be used more effectively to map the processes by which drugs affect the brain and are metabolised.

The emerging technology of MEG (magnetoencephalography) allows events in the brain to be tracked in time and also has high spatial resolution. There is currently only one MEG machine in the UK but more are likely to be installed.

Future targets

Future imaging technology might be used to address problems such as the brain differences that may predispose individuals to substance and behavioural addiction. Another area where it may be used is examining the persistence of neural changes in former addicts, which might allow the very significant issue of relapse to be addressed.

One key target for neurobiology is to translate our knowledge of human genes and the proteins for which they code into human differences such as susceptibility to addiction. Imaging allows the connection between genetic difference and brain structure to be seen directly. Differences between individual drug responses, for example, the different male and female responses to MDMA (ecstasy) are already being explored.

The full version of this review is on www.foresight.gov.uk

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