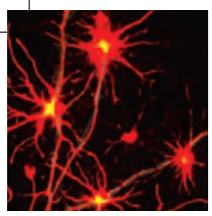

Genomics summary

The genetic makeup of a drug user influences the effects of a drug, including the likelihood of addiction. Knowledge of genetic make-up may have potential to identify the most effective treatment for individuals. In addition, drug use can alter gene function. The application of the findings raise significant ethical issues.

The Foresight project on Brain Science, Addiction and Drugs asked David Ball and David Collier of the Institute of Psychiatry, King's College London, Marcus Pembrey of the Institute of Child Health, University College London and Dai Stephens of the University of Sussex to examine the link between genes and addiction.

The new science of genomics studies the effects of genes in humans and other species. It has been given impetus by our emerging knowledge of the human genome.

Susceptibility

The connection between human genetic variations and the differences between people is contested and likely to remain so. Some characteristics are associated with variations in a single gene, but these are few by comparison with those that involve many genes in varying combinations. In addition, genetic influences. along with environmental, social and other factors may contribute to susceptibility to addiction or other behaviours, rather than determining this susceptibility. Studies of addiction to alcohol, nicotine and controlled drugs show that the genetic contribution to susceptibility to sustained use is between 25 and 60 per cent for a range of substances.

Well-established studies show that a predisposition to alcoholism runs in families, and that there is a genetic element to this susceptibility. Candidate genes and chromosome areas for this susceptibility in humans have been identified, and a similar pattern is seen in some animals. Analogous results have been found in research on smoking.

Most work in this field to date has been related to alcohol. But genetic susceptibilities to substances such as tobacco, opioids, cannabis, sedatives, stimulants and psychedelics have also been found. However, the changing use patterns of different psychoactive substances show that social forces are also a strong influence on their use, and complicate the study of genetic factors.

It may become possible to counsel individuals who are at high risk of addiction in an attempt to help them avoid drug use. It is important not to create the impression that people without an especially risky genotype can use psychoactive substances with impunity.

Vulnerability

The damage caused by drugs varies from person to person. In the case of alcohol, genetic differences appear to underlie widely differing susceptibility to liver damage. Genetic factors also affect the chance of smokers developing lung and other cancers.

But as with susceptibility, it is vital not to allow individuals who are not at severe risk to believe that they can use drugs 'safely'. Smoking and alcohol, for example, each cause a wide range of harms.

Giving up

Variations in individual responses to treatments for drug misuse have been reported. These studies indicate that an individual's genes may influence the effectiveness of various forms of treatment. One of several studies of nicotine independence suggested that variation in genetic reponse to treatment may depend on nicotine metabolism. Genes have also been identified as a factor in unpleasant side-effects of treatment for nicotine dependence in some individuals, with the result that such treatment was less likely to be completed successfully by those individuals. These findings have potential for improving treatment effectiveness, including the reducing the likelihood of relapse following treatment.

Adverse effects of psychoactive substances on child development

Alcohol, nicotine and controlled drugs are known to affect prenatal development. They alter and impair the formation of brain tissue. Fetal exposure to nicotine also seems to increase a chance of addiction to it in later life.

Evidence is now emerging that use of psychoactive substances can also adversely affect development during childhood and adolescence and especially the development of brain. Psychoactive substances can alter gene activity levels at these stages of development.

The future

Progress in this field is rapid. In particular, connections between specific groups of genes, biochemical pathways, and brain areas with which they are involved are likely to become increasingly apparent. Our knowledge of the way in which variations in individuals' genetic makeup contributes to varying reactions to drugs and treatments for drug misuse is certain to grow. Drugs also alter the way genes are expressed, in the brain and the rest of the body, and details of these interactions are likely to emerge over the coming decade.

Transgenerational studies may add a new dimension to drug effects beyond classic inheritance of susceptibility genes from mother and/or father. There is emerging evidence that exposures before puberty, e.g. smoking onset in mid childhood, in one generation can produce adverse effects in the next and subsequent generations. Furthermore these transgenerational responses can occur down both the male and female lines.

Public attitudes to addiction and addicts are certain to be influenced by new knowledge about the contribution of genes to an individual's susceptibility to addiction and response to a particular treatment. These findings are likely to raise questions about ethics which will influence future direction of health policies.

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