

CS01-03

GENETICS OF ADDICTION

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It is well known from twin, family and adoption studies that addictive behaviours are under a degree of genetic influence, which is reflected in moderate to high heritability coefficients for these phenotypes. In the last twenty years, considerable effort has been invested in attempting to determine the molecular genetic basis of this influence, with mixed success. While early candidate gene studies for the most part failed to identify genetic variants which were reliably associated with risk of substance use, more recent genomewide association methods have begun to yield promising findings and novel insights into the mechanisms of addictive behaviours.

The history of genetic studies of risk of substance use will be presented, including a brief overview of twin, family and adoption studies, and of candidate gene and linkage studies. More recent findings, in particular focusing on genomewide association studies, will be discussed in detail. Finally, emerging findings from gene x environment and intermediate phenotype studies will be highlighted. This presentation will provide a comprehensive overview of the current state of the field of addiction genetics, placed in the historical context of heritability, candidate gene and linkage studies.

While the study of the genetics of addictive behaviours remains in relative infancy, some compelling findings are beginning to emerge. Genetic variants which influence the metabolism of specific substances, such as alcohol and nicotine, appear to influence the intake of those substances. A number of genes which encode drug targets also appear to influence drug-taking behaviour, such as the alpha-5 nicotinic acetylcholine receptor subunit, which has been robustly shown to associate with heaviness of smoking. However, the proportion of phenotypic variance explained by these variants remains small. Potential reasons for this will be discussed.