FOREWORD

FOCUS CONTENTS

Addiction: from mechanisms to treatment

It needs no explanation that addiction is an extremely serious problem, considering its impact on both health and society. Unsurprisingly, addiction is a major focus of neuroscience research, and the molecular, cellular and circuit mechanisms underlying addiction are slowly beginning to be understood. Despite these research efforts, few effective treatments exist, highlighting the need for continuing investigation. This Focus on Addiction brings together five articles that review the current state of the field and that point to potential new treatment opportunities.

Much of addiction research focuses on the brain's reward system. A popular idea of addiction is that drugs of abuse 'hijack' this system, disrupting the normal behavioural responses to natural rewards. However, it has been argued that natural rewards can also induce an addiction-like state. For example, the hedonic properties of palatable food can, in some people, lead to dysregulation of food intake, resulting in binge eating and, ultimately, obesity. In his Review, Paul J. Kenny describes how excessive intake of palatable foods and drugs of abuse cause similar molecular, cellular and circuit changes, not only in the reward system but also in the brain stem, hypothalamus and several cortical areas.

Studies in animals and humans have shown that the prefrontal cortex (PFC) has a major influence on drug-taking behaviour, owing to its regulation of reward circuits and its role in executive functions such as self-control. Goldstein and Volkow review a decade's worth of neuroimaging studies on the PFC in addicted individuals. Based on these studies, they present a model of how interactions between dorsal and ventral PFC regions change in the course of the addiction process. Understanding how PFC functioning is altered in addiction may help in the development of new treatments; for example, cognitive–behavioural approaches that target specific PFC functions may prevent relapse.

Relapse can occur after weeks, months or even years of abstinence. Drug-induced long-lasting changes in the transcriptional potential of genes in brain regions involved in reward processing may contribute to this phenomenon, and in their Review, Robison and Nestler examine the evidence for this hypothesis. They show that chronic exposure to drugs of abuse alters the expression or activity of several transcription factors, induces changes in the epigenetic status of several genes through histone tail or DNA modification, and alters the expression of microRNAs in reward regions. Epigenetic changes alter steady-state gene expression but may also influence the inducibility of genes in response to subsequent drug exposure, which — as the authors suggest — could affect the adaptability of the addicted individual.

Current theories of addiction assume that different types of addiction have a common psychobiological substrate. However, as argued in a Perspective article by Badiani and colleagues, it is important to acknowledge that several factors distinguish different types of addiction. Focusing on psychostimulant and opiate addictions, they show that there are numerous cognitive, neurobiological and behavioural differences between these conditions. Such differences have important implications for theories of drug addiction as well as for the development of treatments.

Indeed, despite decades of research into the neurobiological processes that underlie addiction, very few effective treatments exist. Differences between addictions as well as genetic heterogeneity in addicted individuals suggest that there may not be a 'magic bullet'. The fact that addiction is partially heritable points to the potential of pharmacogenetic treatment approaches. In their Review, Heilig and colleagues discuss this issue in the context of alcohol addiction, using naltrexone therapy for alcohol addiction as a case in point. Although initial studies indicated that naltrexone had a small effect size, subsequent studies showed that it is in fact effective in individuals with a particular polymorphism of the mu opioid receptor gene. Genetic variations in the corticotropin-releasing factor, serotonin and GABA systems have also been implicated in alcohol addiction and may become new pharmacotherapeutic targets. As the authors point out, more attention needs to be paid to personalizing pharmacotherapy for alcohol — and other — addictions.

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