Research into addiction explores many aspects of how and why this disease develops. Here are four of the toughest questions.

BY DAVID HOLMES

ADDICTION

4 BIG QUESTIONS

QUESTION

WHY IT MATTERS

WHAT WE KNOW

NEXT STEPS

1

How broadly should we define addiction?

We often think about addiction in connection with the misuse of substances such as alcohol, heroin and cocaine. But should compulsive behaviours that involve sex, video games and gambling also be treated as addictions?

Gambling is the only officially recognized behavioural addiction. But there is increasing evidence that other behaviours resemble substance misuse in their underlying neurobiology, and the way in which they respond to treatment (see page S62).

Researchers want to move from a system that classifies addiction according to clinical symptoms to one more rooted in a mechanistic understanding of the disease, with a greater role for genetic imaging and cognitive science.

2

How is addiction affected by our genes?

A better understanding of the genetic factors that influence the risk of addiction could revolutionize the way that addiction is diagnosed, treated and prevented.

Numerous adoption and twin studies have shown that the risk of addiction is about 50% heritable. But identifying the genetic factors and the extent to which they interact with each other and the environment has been more tricky (S48).

Researchers are looking in ever-finer detail at potential sources of genetic variations (such as gene copy-number or the existence of rare genes) and epigenetic changes in the way that genes are expressed.

3

If addiction rewires the brain, can we short the circuit?

Scientists know that the use of addictive substances causes physical changes in the brain that can lead to addiction. What they are just beginning to understand is how those changes can be reversed to treat the disease.

Using optogenetic-guided brain surgery in mice, researchers have been able to identify a type of dopamine receptor that seems to have a crucial role in addiction. Blocking this receptor has reversed the symptoms of cocaine addiction in mice (S50).

For practical and ethical reasons, optogenetic methods cannot be used in humans, but their increasing use in the lab could speed the discovery of drugs to target and reset the reward circuits that are overloaded in addiction.

4

Can we get from the 12-step recovery programme to one shot?

One of the biggest hurdles in treating addiction is preventing relapse: people can fall off the wagon after years of abstinence. A vaccine that neutralizes a substance before it reaches the brain could prevent people from returning to old habits.

Researchers have been developing anti-drug vaccines for more than two decades and have a candidate that tricks rats' immune systems into thinking injected heroin is a pathogen, so the drug is quickly neutralized before it reaches the brain (S53).

Without a trial of an effective vaccine in humans, concerns over whether a vaccine could lead to drug users taking ever-higher doses cannot be addressed, but few, if any, pharmaceutical companies look likely to stump up the cash.

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