THE HIJACKED BRAIN

Addiction is a devastating disease that alters the brain's circuitry, notably in young adults. But the changes need not be permanent: improved understanding of them will help in developing ways to lessen the burden. By **Margaret Munro**. *See a* Nature *Video at go.nature.com/e1gqkk.*

ADDICTION CYCLE

Addiction is characterized by bingeing, withdrawal, cravings, dysfunctional emotions and an inability to abstain from the substance or behaviour. It quickly leads to disruption of interconnected brain circuits that are involved in reward, learning and control.

With time, other brain areas are recruited, including those involved in stress and anxiety — in effect an 'anti-reward' system.

STAGE 1
BINGE/ INTOXICATION

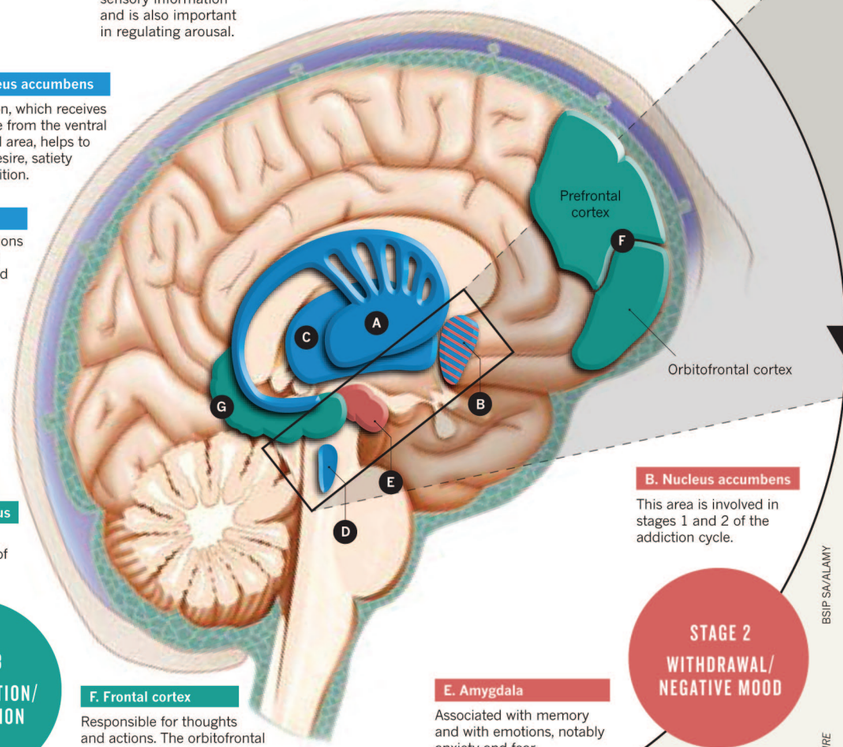
Overstimulation of the reward circuit leads to loss of control and bingeing.

C. Thalamus
Acts as a hub to relay sensory information and is also important in regulating arousal.

D. Ventral tegmental area
A primitive structure at the top of the brain stem in which dopamine is synthesized (see 'The dopamine connection').

B. Nucleus accumbens
This region, which receives dopamine from the ventral tegmental area, helps to control desire, satiety and inhibition.

A. Basal ganglia
Interconnected regions that are involved in learning, reward and habit formation.



G. Hippocampus
Important for consolidation of memory.

B. Nucleus accumbens
This area is involved in stages 1 and 2 of the addiction cycle.

STAGE 3
PREOCCUPATION/ ANTICIPATION

F. Frontal cortex
Responsible for thoughts and actions. The orbitofrontal cortex is thought to play a part in controlling behaviour.

E. Amygdala
Associated with memory and with emotions, notably anxiety and fear.

STAGE 2
WITHDRAWAL/ NEGATIVE MOOD

People with dependencies have compulsive cravings to repeat the addictive behaviour. Drug misuse is thought[2] to alter the function of the frontal cortex (F) and the hippocampus (G) and helps to embed desires even if they have negative consequences.

Chronic exposure to addictive substances and behaviours reduces the number of dopamine receptors in the nucleus accumbens (B), so more of the addictive substance or behaviour is needed to feel normal. Changes to the amygdala (E) circuitry have been tied to the irritability, anxiety and stress associated with withdrawal[1].

BSIP SA/ALAMY

DESIGN BY **MOHAMED ASHOUR**/*NATURE*

27 MILLION
people had problematic drug use[3] in 2012.

183,000
drug-related deaths were reported[3] in 2012.

1 BILLION
or more people smoke, with the majority living in low- to middle-income countries[4].

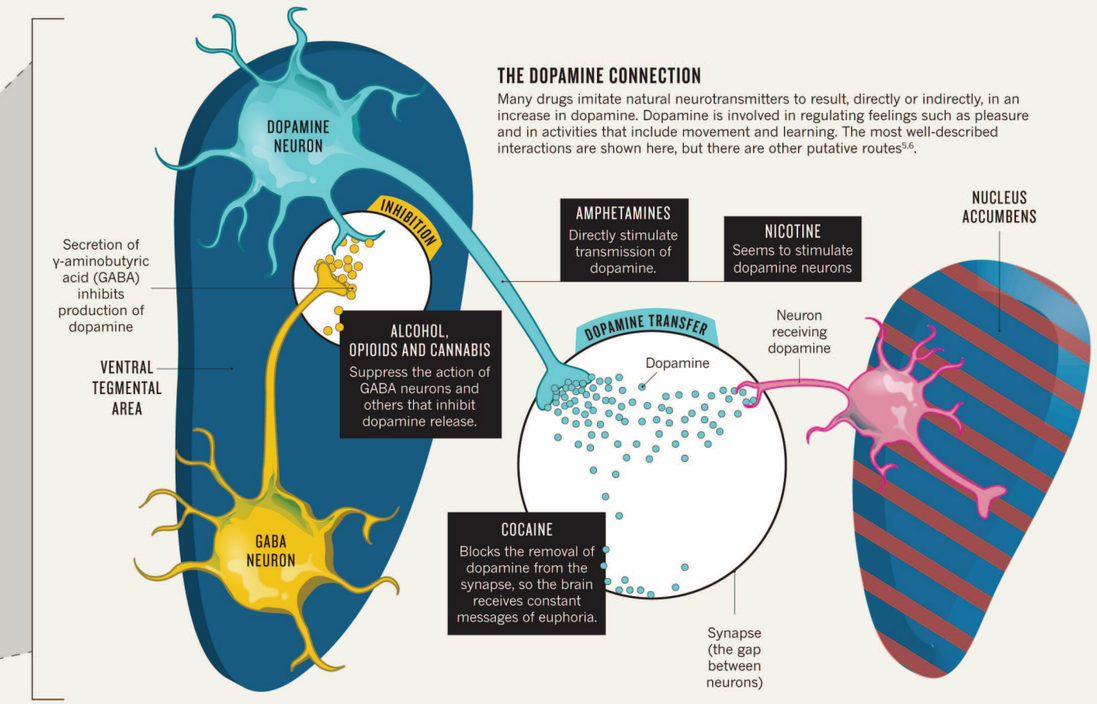
6 MILLION
smokers die every year; more than 5 million of the deaths are directly related to tobacco use[4].

38.3%
of the global population drinks alcohol, with an annual average of 17 litres per person[4].

3.3 MILLION
deaths in 2012 were attributed to alcohol consumption[4].

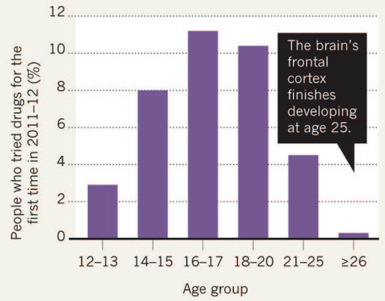
THE DOPAMINE CONNECTION

Many drugs imitate natural neurotransmitters to result, directly or indirectly, in an increase in dopamine. Dopamine is involved in regulating feelings such as pleasure and in activities that include movement and learning. The most well-described interactions are shown here, but there are other putative routes[5,6].



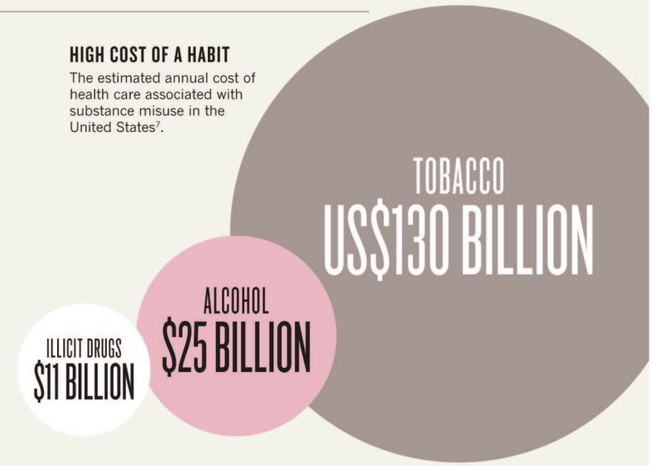
DANGEROUS AGE

Many people have their first experience of drugs at a young age, placing them at high risk of addiction. The developing brain may not form properly under the influence of drugs or alcohol[7].



HIGH COST OF A HABIT

The estimated annual cost of health care associated with substance misuse in the United States[7].



Sources: 1. Logrip, M. L., Koob, G. F. & Zorrilla, E. P. *CNS Drugs* **25,** 271–287 (2011); 2. Schoenbaum, G. & Shaham, Y. *Biol. Psychiatry* **63,** 256–262 (2008); 3. United Nations Office on Drugs and Crime *World Drug Report 2014* (United Nations, 2014); 4. World Health Organization; 5. Nestler, E. J. *Nature Neurosci.* **8,** 1445–1449 (2005); 6. Flagel, S. B. *et al. Nature* **469,** 53–57 (2011); 7. US National Institute on Drug Abuse.