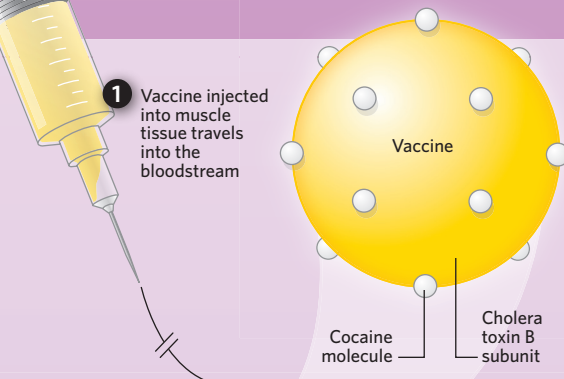
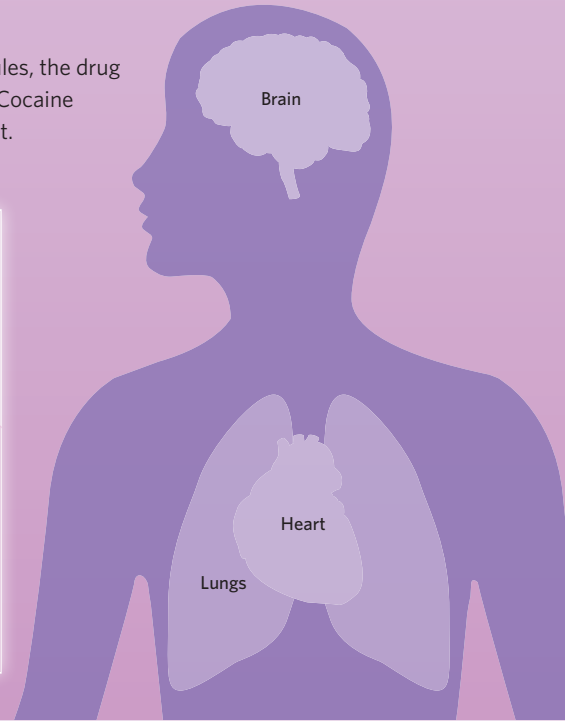
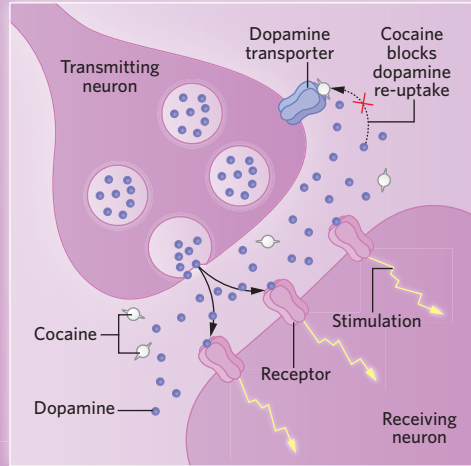


THE ANATOMY OF A HIGH

When someone snorts or smokes cocaine, which is composed of small crystalline alkaloid molecules, the drug enters the bloodstream and from there eventually crosses into the heart, brain, and other organs. Cocaine quickens heart and respiratory rates, but it is in the brain that the drug has its most dramatic effect.

Once cocaine molecules have crossed the blood-brain barrier, they bind tightly to dopamine transporter proteins embedded in the membranes of presynaptic neurons, preventing these molecular pumps from performing their role of clearing dopamine from the synaptic cleft back into storage vesicles inside the neuron. As dopamine, a potent neurotransmitter, accumulates in the synaptic cleft, dopamine receptors on the postsynaptic neuron are continuously stimulated, creating a euphoric state that users report as a "high." As cocaine is metabolized and cleared from the brain, dopamine levels drop drastically, typically resulting in a dysphoric state or "low." With prolonged and consistent use of the drug, dopamine receptors disappear from the surface of neurons, causing addicted users to ingest more cocaine to attain a satisfactory high.



VACCINATING AGAINST ADDICTION

The cocaine vaccine uses the body's immune system to prevent the drug from reaching dopamine transporters in the brain. The vaccine, which comprises several cocaine molecules bound to a recombinant cholera toxin B subunit along with an adjuvant, is injected into the patient's muscle **1**. Vaccine particles make their way into the bloodstream, where they are taken up by immune cells that activate plasma cells into producing antibodies specific to the cocaine molecules conjugated to the cholera toxin **2**. If cocaine enters the bloodstream after vaccination, the anti-cocaine antibodies will bind to the molecules, making the conglomerate too bulky to fit through the narrow gaps formed in the tight junctions between cells at the blood-brain barrier. This prevents cocaine from interfering with dopamine transporter receptors and causing the buildup of dopamine perceived as a high **3**. The antibody-bound cocaine molecules are then broken down in the liver and bloodstream with the help of an enzyme called cholinesterase, yielding an inert metabolite, benzoyllecognine, which does not bind to the cocaine antibodies and is flushed from the body **4**.

