NATURE | VIDEO

Transparent brains reveal effects of cocaine and fear

Circuits that respond to addiction and terror are modelled in three dimensions.

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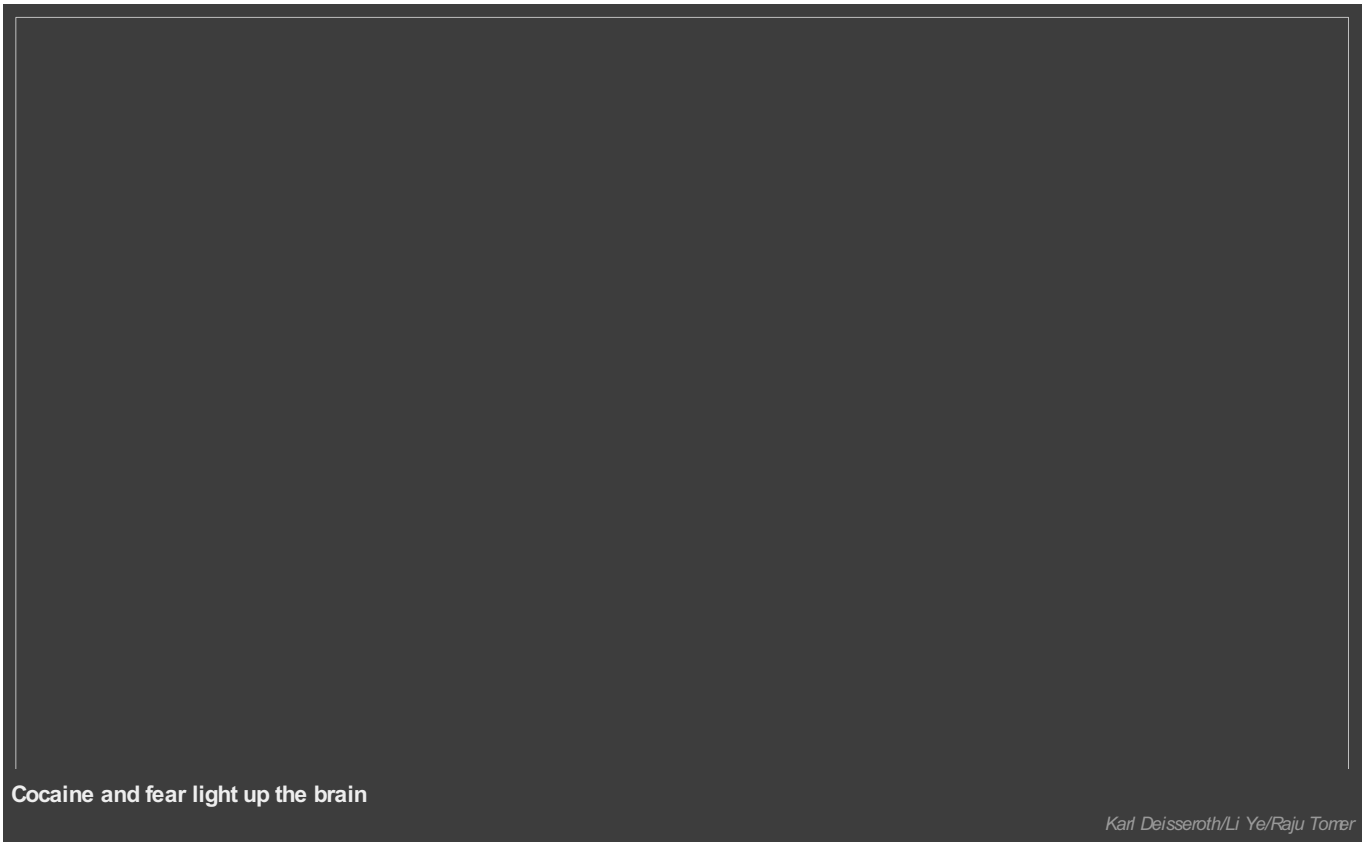

Cocaine and fear light up the brain

Karl Deisseroth/Li Ye/Raju Tomer

A technique that makes mouse brains transparent shows how the entire brain responds to cocaine addiction and fear. The findings could uncover new brain circuits involved in drug response.

In the technique, known as CLARITY, brains are infused with acrylamide, which forms a matrix in the cells and preserves their structure along with the DNA and proteins inside them. The organs are then treated with a detergent that dissolves opaque lipids, leaving the cells completely clear.

To test whether CLARITY could be used to show how brains react to stimuli, neuroscientists Li Ye and Karl Deisseroth of Stanford University in California engineered mice so that their neurons would make a fluorescent protein when they fired. (The system is activated by the injection of a drug.) The researchers then trained four of these mice to expect a painful foot shock when placed in a particular box; another set of mice placed in the box received cocaine, rather than shocks.

Once the mice had learned to associate the box with either pain or an addictive reward, the researchers tested how the animals' brains responded to the stimuli. They injected the mice with the drug that activated the fluorescent protein system, placed them in the box and waited for one hour to give their neurons time to fire.

The next step was to remove the animals' brains, treat them with CLARITY, and image them using a system that could count each fluorescent cell across the entire brain (see video). A computer combined these images into a model of a three-dimensional brain, which showed the pathways that lit up when mice were afraid or were anticipating cocaine.

Deisseroth says that it is increasingly apparent that complex behaviours such as addiction are due to connections and cross-talk between different parts of the brain, rather than activity in a single area.

Ye presented the results on 14 November at the conference of the US National Institute on Drug Abuse in Bethesda, Maryland. He says that the group now plans to engineer mice so that the pathways identified in this research can be activated by a flash of light, to see whether this causes the mice to act as if they are fearful or happy.

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