TOOLBOX

Deep-brain neurons' glow reveals elements of social circuits

BY **KATE YANDELL**

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Light-transmitting cables implanted deep in mouse brains reveal connections between brain regions that control social interactions, according to a study published 19 June in *Cell*[1].

Researchers used the new method, called fiber photometry, to record brain activity in awake mice as they moved around cages.They discovered that neurons connecting two brain regions associated with **reward** are active when female mice socialize with other female mice.

The researchers **presented work on fiber photometry** at the **2013 Society for Neuroscience annual meeting**. In the new paper, they showed how **optogenetics**, a way to activate genetically engineered neurons by stimulating them with light, complements fiber photometry.

Scientists can already engineer neurons so that they light up when they fire, illuminating how neural circuits behave under natural circumstances.

Methods for detecting neural firing in alert mice are primarily useful close to the brain's surface, however. They detect activity in the cell bodies of neurons, where the glow is relatively strong, rather than out near the **synapses**, where neurons talk to each other. Recording activity in axons, the long segments of neurons that carry signals out to synapses, is key to understanding how brain regions are connected.

In the new study, the researchers surgically inserted the same type of thin fiber-optic cables into mouse brains that are used in optogenetics to stimulate neurons.This is a relatively noninvasive way to reach deep into the brain.In fiber photometry, these cables funnel light back from firing neurons to an external sensor.

To detect the faint light signals from axons, the researchers used a type of amplifier that can separate weak signals from noise as long as the signal is at a known wavelength.They arranged the sensors so that they were tethered to the mice by long cables, allowing the mice to move around relatively naturally even when hooked into the system.

This new system can be used to investigate any number of neural circuits, but the researchers opted to first look into non-aggressive, nonsexual social interactions.

They placed an unfamiliar female mouse in a cage alongside a female mouse fitted with a fiber-optic probe, and recorded neural activity emanating from theventral tegmental area (VTA), adeep-brain region involved in reward.VTA neurons connect to multiple brain regions, including another reward region called the nucleus accumbens.

The researchers found that the axons that lead to the nucleus accumbens light up in the presence of an unfamiliar mouse but show much less activity in the presence of an object such as a plastic ball or wooden block.

Using optogenetics, they then found that forcing VTA neurons to fire stimulates neurons in two regions, the nucleus accumbens and the medial prefrontal cortex.And activating VTA neurons that connect to the nucleus accumbens makes mice more apt to socialize, indicating that these neurons are involved in social behaviors. In contrast, activating neurons leading to the medial prefrontal cortex does not affect social behavior.

It is unclear exactly why the path from the VTA to the nucleus accumbens is important, but the researchers hypothesize that activating it may motivate the mice to socialize,whereas other networks control more cognitive aspects of the interaction.

REFERENCES:

1. Gunaydin L.A. *et al*. *Cell* **157**, 1535-1551 (2014) **PubMed**