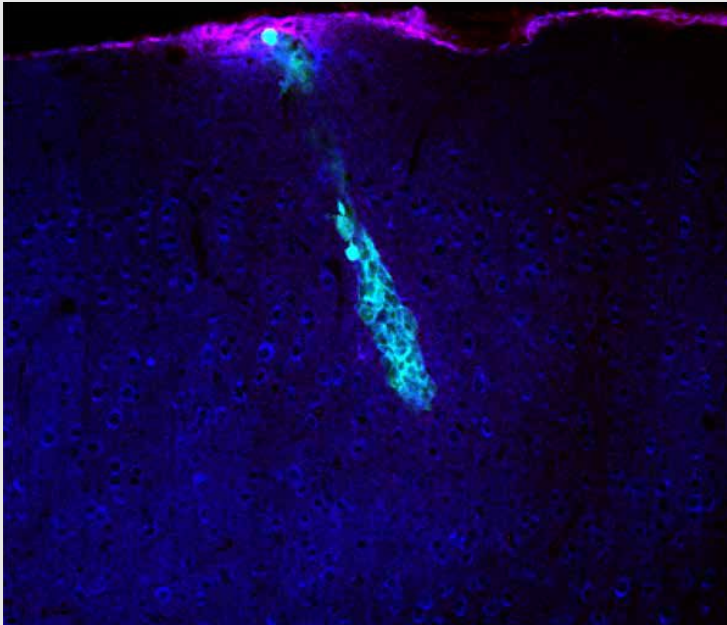


Sensors shed light on levels of chemical messengers in mice

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Telltale trace: Cells modified to fluoresce in the presence of dopamine and norepinephrine are visible (in blue-green) seven days being injected into a mouse brain.

Cells modified to carry a fluorescent sensor can help researchers detect the levels of various chemical messengers in the brains of living mice.

The tool, described 26 October in *Nature Methods*, distinguishes between dopamine and norepinephrine, two **neurotransmitters** involved in learning and memory¹. It could be adapted to detect neurotransmitters relevant to specific conditions, such as autism, the researchers say.

Signals in the brain are passed from one neuron to another through the junctions, or **synapses**, that separate them. This can happen quickly — through fast-acting neurotransmitters that trigger neurons to fire — or slowly, through a more complex sequence of molecules.

The slow signaling, which can occur in a matter of seconds, is involved in **changes in neuron connections** that enable

learning, **memory** formation and decision-making.

In order to detect the neurotransmitters, the researchers engineered cell lines to express a protein that binds either dopamine or norepinephrine. They then injected those cells, called CNiFERS (pronounced ‘sniffers’), into the mouse brain. When the cell’s receptors detect the neurotransmitter, they trigger an influx of calcium ions into the cell. And the rising calcium levels set off the fluorescent reporter, signaling the presence of the neurotransmitter.

Both CNiFERS fluoresce the same combination of yellow and blue green, but the researchers tell them apart by injecting the dopamine and norepinephrine versions in a slightly different site within the same brain region. Their brightness indicates the level of the neurotransmitter present.

CNiFERS can be injected into the brains of living mice, and a window cut into the mouse’s skull allows researchers to measure the fluorescence in real time. To test how well the reporters work, the researchers measured both dopamine and norepinephrine signals in the frontal cortex of mice as the animals learned to associate a sound with a sweet drink.

Mice that learned to associate the two events released a pulse of dopamine in anticipation of the sweet reward when they heard the tone, but didn’t show a change in norepinephrine.

Researchers had suspected this link between dopamine and reward anticipation, but had yet to observe the neurotransmitter release in real time.

The researchers next plan to create CNiFERs to detect other chemical messengers, such as somatostatin. They could also use the system to investigate neurotransmitters relevant to certain conditions — for example, the balance between excitatory and inhibitory signals, which **may be altered in people with autism**.

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References:

1. Muller A. *et al. Nat. Methods* Epub ahead of print (2014) PubMed