NEURAL CIRCUITS

Virtual reality & the time-telling mouse

Heys, J.G. and D.A. Dombeck. *Nat. Neurosci.* **21**, 1574–1582 (2018)

Do your mice know what time it is? Possibly, says new research from Northwestern University about the neural circuits that may underlie temporal awareness in rodents.

Humans can obviously tell time, says senior author Daniel Dombeck, as can nonhuman primates. Rodents just might be able to too, but asking a mouse how long it has been waiting around has been technically challenging. Are they really judging time, or other uncontrolled-for variables?

Enter virtual reality. The technology allows researchers to control the world an animal is behaving in, and, with head-fixed mice and two-photon microscopes, record cellular-resolution images of neuronal activity as the animals navigate that virtual space. “We can do things in virtual reality that you just can’t do in real environments,” Dombeck says.

Like make invisible obstacles. In research published in *Nature Neuroscience*, Dombeck

and postdoctoral fellow James Heys created a virtual ‘door stop’ task to gauge whether their mice had an internal sense of time. The mice were trained to run on a treadmill while viewing a virtual corridor, at the end of which waited their water reward. About half way down the corridor, Heys and Dombeck then added a virtual door. The mice had to stop and wait six seconds for the door to open before they could continue on their way.

Once the mice got the hang of it, the door was made invisible. When the mice reached its location, they *could* keep moving their feet, but they would not visually progress until the invisible door opened. With nothing physical to see, hear, or even smell, they instead had to rely on an internal sense of time to accomplish the task.

While the mice were waiting, Heys and Dombeck were watching neurons in the medial entorhinal cortex (MEC), a region of the brain that sits above the hippocampus

and has been linked to the encoding of episodic memory. “Lo and behold, when the animals were resting, when they stopped, a new set of neurons that nobody had seen before turned on,” says Dombeck. Those neurons, he says, could be read like a clock: one subset of neurons in the MEC would fire after one second had elapsed, another after two seconds, and so on through the six-second waiting period. “This is a correlation with time,” he says. “Just the fact that the animals could do this was a bit surprising.”

To determine if there is a causal relationship and whether the circuitry is unique to the MEC, the lab plans to inactivate those neurons and see how that impacts the animals’ ability to learn the virtual door stop task.

Time will tell.

Ellen P. Neff

Published online: 3 December 2018
<https://doi.org/10.1038/s41684-018-0206-5>

INSTECH

Oral gavage, refined.

Our plastic feeding needles have flexible tubes with soft tips to reduce trauma, and they're disposable to eliminate the hassle of cleaning.

Available in a range of sizes for mice, rats and other rodents.

www.instechlabs.com

Not sure which size you need?
 Request free samples at www.instechlabs.com

3R.