'Free lunch' warps inner spatial map in rat brains and, by implication, human brains

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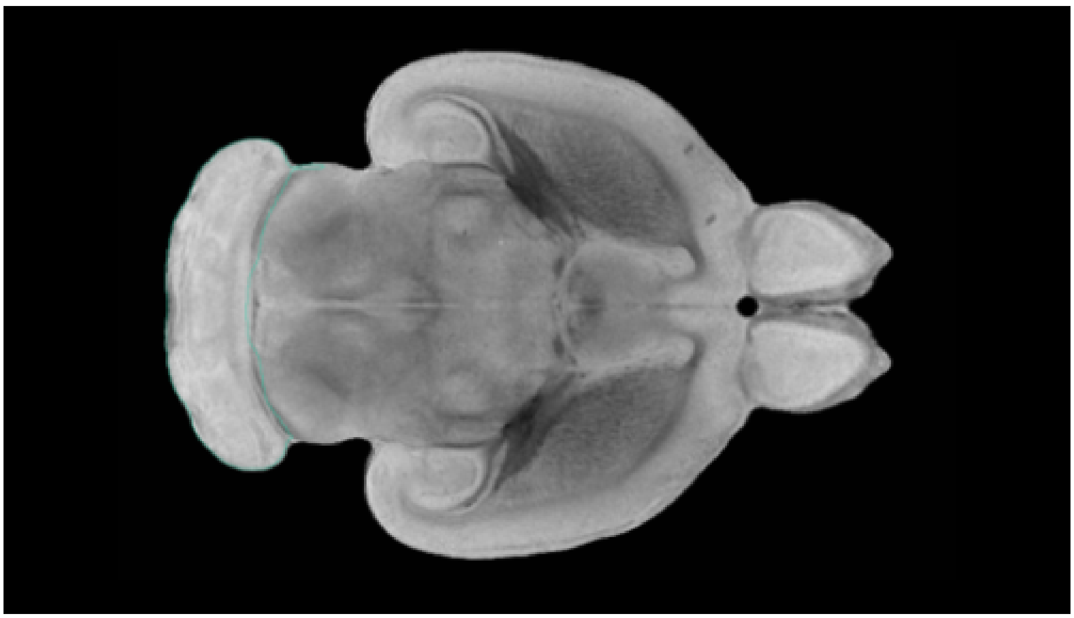

Cerebellum of CIVM postnatal rat brain atlas. Credit: Neurolex

The next time you're offered a free sample as you're walking past a storefront, go ahead and take it. But be aware that the more you like that little chunk of cheese or sip of herbal tea, the likelier your brain's internal map will warp in a way that increases your ability to return to the spot where you got your freebie.

Our brains' neural circuitry creates spatial maps as we navigate through new environments, allowing us to recall locations and directions. While it's been known for some time that we have these internal maps, a study from the Stanford University School of Medicine to be published online March 29 in *Science* shows how, in rats, those maps get redrawn when the rats learn they'll receive a reward at a certain place on the map. This same process could play a role in addictive behavior in humans.

Lisa Giocomo, Ph.D., assistant professor of neurobiology, is the study's senior author. Lead authorship is shared by postdoctoral scholar William Butler, Ph.D., and graduate student Kiah Hardcastle.

"Every time you check your Google map for a particular address or restaurant name or pair of grid coordinates, you get the same map regardless of why you're looking at it," Giocomo said. "The global positioning system that generates that map doesn't care what you're doing or where you're going, or whether you're happy, hungry or hung over. It's always going to give you the same information."

Scientists have assumed the brain's internal GPS operates similarly. But it turns out that's not quite right.

"In this study, we've learned your internal map changes depending on your behavior, memories and state of mind," Giocomo said. "We pull up different maps for the same space, depending on what we're actually trying to do in that space."

Brain area crucial to navigation

Giocomo's research has been focused on a brain area called the medial entorhinal cortex, which is crucial to navigation. Nestled near the center of the human brain, it integrates information from our senses to generate maps of new places.

Over the past 15 years or so, scientists have learned that various nerve cells in our medial entorhinal cortex act as compasses, speedometers, latitude and longitude coordinates, or boundary and landmark detectors. These cells have been identified in rodents, bats, monkeys and humans, suggesting that such spatial-mapping circuitry is a universal mechanism of mammalian navigation and that the findings in the study apply to humans as well.

Until now, all indications have been that it's just that simple. But that's because the experiments designed to capture and measure the mapping process have been deliberately kept simple, for the sake of getting decipherable results. A standard experimental setup, for example, features a spacious yet simple environment: a big, open-top box in which the floor is littered with bits of crushed cereal. No consideration is given to the test animals' mood or intent. The animals can walk freely all around the box, foraging at their leisure for crushed Cheerios, while researchers collect data via physiological monitoring of the creatures' brain cells. It is a relatively easy experiment to do. The scientists who thought it up won a Nobel Prize for it in 2014. (The work was done under the leadership of a pair of Norwegian researchers under whom Giocomo did her postdoctoral fellowship.)

"But animals don't typically walk around inside big black boxes in the hope of hoovering up Cheerios dust," Giocomo said. "You usually have a goal. So we decided to design a situation that would stimulate that goal-directedness but would also be able to relate whatever we found to what had been studied for the past 15 years."

A new box

That meant shifting experimental animals between two alternate environments, one encouraging random meandering and the other one fostering goal-driven behavior. To test goal-driven behavior, Giocomo and her colleagues designed a big box that was exactly the same size and shape as the one in the traditional experimental setup. Both boxes had floors with randomly scattered crushed Cheerios. During experiments in either box, animals could forage freely and eat any Cheerio bits they found. But there was an important difference. The second box had an unmarked, roughly 8-by-8-inch "reward zone" in a fixed location on its Cheerios-strewn floor. The test animals were permitted to forage freely in this box, just as in the other one. But they soon learned that if, in response to an auditory cue, they navigated to the reward zone, they'd get a guaranteed, good-sized crushed-cereal reward. This reward was available only intermittently, and only for a short period after the cue.

Picture a "free lunch" counter in a supermarket. The counter is only open some of the time—but when it is, a storewide advertisement blares the news to hungry shoppers over the public address system.

The investigators implanted electrodes in several hundred nerve cells in the medial entorhinal cortex of rats that were placed in each of the two environments. The electrodes were connected to long cables, so the researchers could monitor individual nerve cells' electrical activity as the animals roved freely inside whichever box they were put in.

"Rats' spatial mapping system is the same as ours," Giocomo said. "For rodents, they're pretty smart. They like to move around. And they love Cheerios."

Giocomo's team collected and analyzed massive amounts of data, which enabled them to identify individual cells in each rat's medial entorhinal cortex that served as compasses, speedometers and position detectors. They also observed that once a rat had learned enough about how the two environments differed—mainly, that one featured an occasional, well-advertised "free lunch"—several types of spatial-map-related cells in its medial entorhinal cortex changed their firing patterns whenever the animal got close to the "lunch counter." For example, as the rats came within about a foot of the center of the reward zone, whether or not the free-lunch counter was open, its position-signifying cells fired faster, and the position-signifying cells that were firing were spaced closer together, indicating higher spatial resolution.

"This tells us the rat's brains are making a new map of space, in response to their experience of a reward, that reflects the importance of the place where they got it by providing a more accurate representation of its position," Giocomo said. If the reward is a drug of abuse, she said, the improved accuracy at the center of this reward-based map could enable an addict's habit.

So the next time you find yourself wending your way through some nondescript side street in a strange neighborhood in search of a parking spot, remind yourself to gobble a chunk of chocolate as you're getting out of your car. It might make it easier for you to remember where you parked.

More information: W.N. Butler el al., "Remembered reward locations restructure entorhinal spatial maps," *Science* (2019). science.sciencemag.org/cgi/doi … 1126/science.aav5297

"Neural representations across species," *Science* (2019). science.sciencemag.org/cgi/doi … 1126/science.aaw8829

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