Medical Xpress

# Scientists reveal complexity in the brain's wiring diagram

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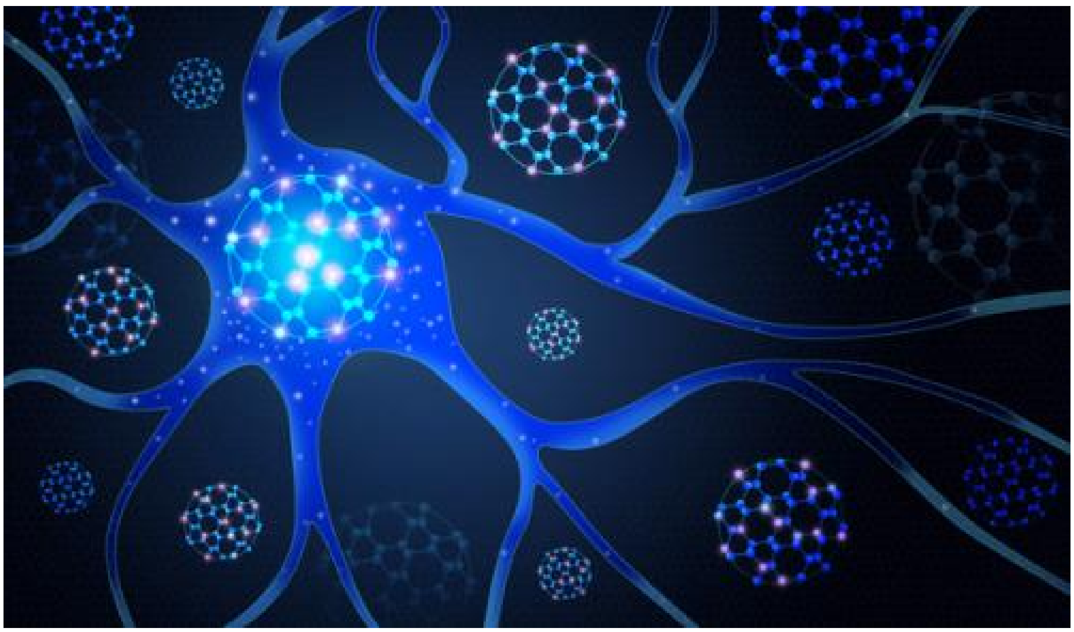

Stanford Bio-X researchers raised an entirely new set of questions when they sought answers about connections between two brain regions.

(Medical Xpress)—When Joanna Mattis started her doctoral project she expected to map how two regions of the brain connect. Instead, she got a surprise. It turns out the wiring diagram shifts depending on how you flip the switch.

"There's a lot of excitement about being able to make a map of the brain with the idea that if we could figure out how it is all connected we could understand how it works," Mattis said. "It turns out it's so much more dynamic than that."

Mattis is a co-first author on a paper describing the work published August 27 in the *Journal of Neuroscience*. Julia Brill, then a postdoctoral scholar, was the other co-first author.

Mattis had been a graduate student in the lab of Karl Deisseroth, professor of bioengineering and of psychiatry and behavioral sciences, where she helped work on a new technique called optogenetics. That technique allows neuroscientists to selectively turn parts of the brain on and off to see what happens. She wanted to use optogenetics to understand the wiring of a part of the brain involved in spatial memory – it's what makes a mental map of your surroundings as you explore a new city, for example.

Scientists already knew that when an animal explores habitats, two parts of the brain are involved in the initial exploring phase and then in solidifying a map of the environment – the hippocampus and the septum.

When an animal is exploring an environment, the neurons in the hippocampus fire slow signals to the septum, essentially telling the septum that it's busy acquiring information. Once the animal is done exploring, those same cells fire off intense signals letting the septum know that it's now locking that information into memory. The scientists call this phase consolidation. The septum uses that information to then turn around and regulate other signals going into the hippocampus.

"I wanted to study the hippocampus because on the one hand so much was already known – there was already this baseline of knowledge to work off of. But then the question of how the hippocampus and septum communicate hadn't been accessible before optogenetics," Mattis said.

Neurons in the hippocampus were known to fire in a rhythmic pattern, which is a particular expertise of John Huguenard, a professor of neurology. Mattis obtained an interdisciplinary fellowship through Stanford Bio-X, which allowed her to combine the Deisseroth lab's expertise in optogenetics with the rhythmic brain network expertise of Julia Brill from the Huguenard lab.

Mattis and Brill used optogenetics to prompt neurons of the hippocampus to mimic either the slow firing characteristic of information acquisition or the rapid firing characteristic of consolidation. When they mimicked the slow firing they saw a quick reaction by cells in the septum. When they mimicked the fast consolidation firing, they saw a much slower response by completely different cells in the septum.

Same set of wires – different outcome. That's like turning on different lights depending on how hard you flip the switch. "This illustrates how complex the brain is," Mattis said.

Most scientific papers answer a question: What does this protein do? How does this part of the brain work? By contrast, this paper raised a whole new set of questions, Mattis said. They more or less understand the faster reaction, but what is causing the slower reaction? How widespread is this phenomenon in the brain?

"The other big picture thing that we opened up but didn't answer is: How can you then tie this back to the circuit overall and learning memory?" Mattis said. "Those would be exciting things to follow up on for future projects."

**More information:** "Frequency-Dependent, *Cell* Type-Divergent Signaling in the Hippocamposeptal Projection." Joanna Mattis, et al. The *Journal of Neuroscience*, 27 August 2014, 34(35): 11769-11780; DOI:

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