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Researchers unravel brain's wiring to understand memory

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Using a powerful microscope, Karel Svoboda, a brain scientist at the Janelia Farm Research Campus in Ashburn, Va., peers through a plastic window in the top of a mouse's head to watch its brain's neurons sprout new connections -- a vivid display of a living brain in action.

Ryan LaLumiere, a neurologist at the Medical University of South Carolina in Charleston, trains cocaine-addicted rats to suppress their craving -- a technique he says may help human addicts.

Elizabeth Kensinger, the director of a neuroscience lab at Boston College, uses an MRI machine to picture the brains of Boston College hockey players as they remember high points and low points from the hockey season -- the better to understand the effect of strong emotions on memory.

These are a few of the cutting-edge experiments that neuroscientists are performing in the latest efforts to understand the mysteries of how the brain learns, remembers and forgets.

The work is shedding new light on how the brain handles memory storage, loss, fear, addiction and aging. Some explore the role of sleep -- even a brief nap -- in consolidating long-term memories. Others are building colorful wiring diagrams, nicknamed "Brainbows," that use different shades to show which neurons connect with which.

The human brain contains some 100 billion neurons that are connected by an elaborate network of tiny wires called axons and dendrites. Neurons communicate by passing chemical signals from axons to dendrites at junctions known as synapses. The sender neuron sends a chemical transmitter, called glutamate, across the synaptic gap. The receiver neuron responds by firing a tiny jolt of electricity.

"The complex thoughts and emotions of our minds are generated in the brain by complex networks of such signal cascades, similar to the electric pulses in a computer," T.S. Thorsen, a Danish researcher, said at the Society for Neuroscience's annual meeting in Washington in November.

"The central mechanism by which the brain works is the release of a substance called glutamate from nerve ends, which is then sensed by neighboring cells," Thorsen said.

The brain responds to life experiences by adjusting the strength of individual synapses and by changing the pattern of connections between neurons. Scientists say this "plasticity" of the brain is the key to how animals and people learn, remember and forget.

Researchers are discovering how to track these changes. For instance, Peter Serrano, a neuroscientist at the State University of New York in Brooklyn, found that a certain molecule, PKM-zeta, increases when a rat learns a memory task, such as how to find its way through a maze.

"For the first time, we can detect a molecular memory trace -- the persistent increased levels in PKM-zeta that last for a month after training," Serrano told the neuroscience conference.

Much memory research is performed on mice, rats and other mammals because it's often impossible to do such work on living humans.

Svoboda, the scientist who watched neurons make new connections inside a mouse brain, said the same thing probably happens in people when they learn a new skill such as typing or playing the piano.

Researchers are gaining new insights into various processes and problems of memory. For example:

• Alzheimer's disease:

Li-Huei Tsai, the director of the Picower Institute for Learning and Memory in Cambridge, Mass., found a gene, HDAC2, in mice, that she said is a prime target for a drug that could treat, or even reverse, the effects of Alzheimer's. She was able to restore lost memories in mice that had been drugged to produce Alzheimer's-like symptoms.

"This is exciting because more potent and safe drugs can be developed to treat Alzheimer's and other cognition diseases by targeting this HDAC specifically," Tsai reported in the journal Nature in May.

"The recovery of long-term memory (in mice) was really the most remarkable finding," she reported. "It suggests that memories are not really erased in such disorders as Alzheimer's, but that they are rendered inaccessible and can be recovered."

• Fear and other emotions:

Kensinger, the Boston College researcher, wrote that "emotion influences every phase of memory. It affects where we direct our attention as we initially experience an event. It influences how the event becomes solidified in our memories over sleep-filled delays, and it molds the ways in which the event is later retrieved."

A recent discovery is the formation of "perineural nets," networks of proteins surrounding neurons that make it hard to erase the memory of fearful events. So far, these nets have been studied only in rodents, but researchers think they may apply to humans, such as soldiers suffering from post-traumatic stress disorder.

• Sleep:

Scientists have long known that sleep plays an important role in consolidating memories and transferring them to long-term storage in the brain.

"Not only do we need to remember to sleep, we need to sleep to remember," said Robert Stickgold, a neuroscientist at Harvard Medical School in Boston.

Recent work by William Fishbein, a psychologist at City College of New York, showed that even "a brief daytime nap" improves memory. College students who napped did better on a memory test than those who stayed awake all day, he said.

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