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Researchers identify mechanism behind associative memory by exploring insect brains

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Researchers at Caltech used locusts to explore connections in the brain that change to form new and specific memories of smells. Credit: Stijn Cassenaer/California Institute of Technology

A key feature of human and animal brains is that they are adaptive; they are able to change their structure and function based on input from the environment and on the potential associations, or consequences, of that input. For example, if a person puts his hand in a fire and gets burned, he learns to avoid flames; the simple sight of a flame has acquired a predictive value, which in this case, is repulsive. To learn more about such neural adaptability, researchers at the California Institute of Technology (Caltech) have explored the brains of insects and identified a mechanism by which the connections in their brain change to form new and specific memories of smells.

"Although these results were obtained from experiments with insects, the components of the mechanism exist also in vertebrate, including mammalian, brains which means that what we describe may be of wide applicability," says Stijn Cassenaer, a Broad Senior Research Fellow in brain circuitry at Caltech and lead author of a paper—published in the journal *Nature* on January 25—that outlined the findings. The study focused on insects because their nervous systems are smaller, and thus likely to reveal their secrets sooner than those of their vertebrate counterparts.

To home in on sensory memories, the researchers concentrated on olfaction, or the sense of smell. When a person encounters a favorite food or the perfume of a loved one, she will typically experience a recall, usually positive, based on the memories evoked by those smells. Such a recall—to a smell, sound, taste, or any other sensory stimulus—is evidence of "associative" learning, says Gilles Laurent, a former professor of biology at Caltech and senior author of the study, as learning often means assigning a value, such as beneficial or not, to inputs that were until then neutral. The original, neutral stimulus acquires significance as a result of being paired, or associated, with a reinforcing reward or punishment—in this case, the pleasant emotion recalled by a smell.

"When we learn that a particular sensory stimulus predicts a reward, there is general agreement that this knowledge is stored by changing the connections between particular neurons," explains Cassenaer. The problem, however, is that the biological signals that represent value (positive or negative) are broadcast nonspecifically throughout the brain. How then, are they assigned specifically to particular connections, so that a certain sensory input, until then neutral, acquires its new, predictive value? "In this study, we carried out experiments to investigate how the brain identifies exactly which connections, out of an enormously large number of possibilities, should be changed to store the memory of a specific association."

To get a closer look at these connections, Cassenaer and Laurent—who is now director at the Max Planck Institute for Brain Research in Germany—measured neural activity in an area of the locust brain where olfactory memories are thought to be stored. They found that what allows the brain to identify which synapses should be modified, and thus where the nonspecific reward signal should act, is a very transient synchronization between pairs of connected neurons.

"When pairs of connected neurons fire in quick succession, the strength of their connection can be altered. This phenomenon, called spike-timing dependent plasticity, has been known for many years. What is new, however, is recognizing that it also makes these connections sensitive to an internal signal released in response to a reward," says Cassenaer. "If no reward is encountered, the cells' sensitivity fades. However, if the sensory stimulus is followed by a reward within a certain time window, then these connections are the only ones altered by the internal reward signal. All other connections remain unaffected."

Laurent says that the molecular underpinnings of this phenomenon, as well as the process by which the stored memories are later read out, are an area of much-needed exploration.

"We are currently developing the necessary tools to examine this with sufficient specificity, which will allow us to evaluate animals' behavior as they learn," says Cassenaer.

More information: "Conditional modulation of spike-timing-dependent plasticity for olfactory learning," *Nature*, Jan 25, 2012.

Provided by California Institute of Technology

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