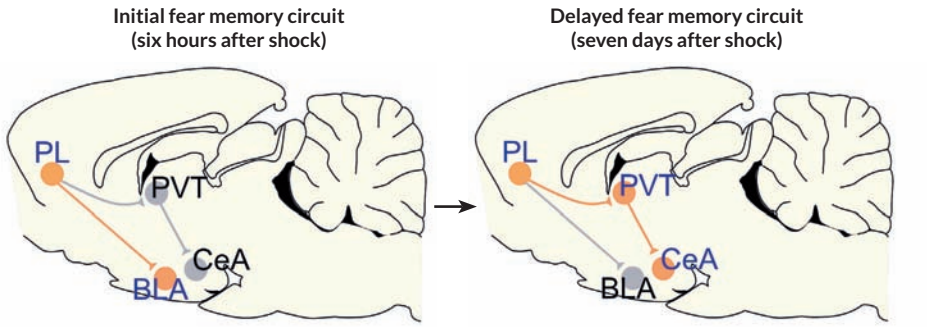
BODY & BRAIN

Memories of fear shift in the brain

Newfound neural circuit may shed light on anxiety disorders

BY ASHLEY YEAGER



In rats, a memory of a shock is initially recalled through connections between brain cells in the prefrontal cortex (PL) and the basolateral amygdala (BLA). A week later, the same fear memory is remembered through a different circuit that connects neurons in the paraventricular nucleus of the thalamus (PVT) with neurons in the central amygdala (CeA).

A newly identified set of brain connections plays an important role in how fear memories are stored and recalled, studies of rodents suggest. The discovery may lead to a better understanding of post-traumatic stress disorder and other anxiety problems.

Two teams of researchers independently found the brain-cell circuit while studying rodents' ability to recall a fear memory. The circuit that initially recalled the memory differed from the circuit that retrieved the memory days later, the researchers report in two papers online January 19 in *Nature*. It is the first time scientists have shown that a memory can be on temporary hold in one area of the brain and later released to a completely separate spot.

"This may be the tip of the iceberg in understanding these types of brain events, suggesting that our concept of memory storage in broad terms may require revision," says Aryeh Routtenberg, a neuroscientist at Northwestern University in Evanston, Ill.

> "Our concept of memory storage in broad terms may require revision."
>
> ARYEH ROUTTENBERG

Storing and remembering a memory requires nerve cells, also called neurons, to talk to each other. Neurons send messages using molecules and electrical signals, linking different brain regions in a setup similar to an electrical circuit.

The idea that memories shift within regions of the brain is not new. Observations of the famous amnesiac Henry Molaison, known as H.M., and other patients suggested that where memories were stored in the brain changed with time (*SN Online: 1/28/14*). In the new research, scientists pinned down precisely when and where a specific memory moved, discovering the previously unidentified circuit in the process.

One team, led by neuroscientist Gregory Quirk of the University of Puerto Rico School of Medicine in San Juan, trained rats to fear a tone that came with a mild shock. Tracking which neurons later turned on in response to the tone revealed which brain circuits the rats used to remember the shock.

Initially the rats' brains recalled the memory by turning on neurons in the brain's frontal lobe, which controls actions and complex thoughts. A set of frontal lobe neurons activated another set of neurons located in a subsection of the amygdala, the brain's fear-processing center. That circuit, however, was not involved in retrieving the memory the next day. Instead, the memory was recalled through a circuit that links the frontal lobe to a region that plays a role in sensing and sleep. This region, located near the brain stem and called the paraventricular nucleus of the thalamus, or PVT, turned out to have a strong connection to a distinct group of neurons in the amygdala.

The scientists then used optogenetics, a technique for controlling neurons with light, to switch off the PVT neurons linked to the amygdala. If the PVT neurons were switched off six hours after storing a fear memory, the rats could still remember their fear of the shock. But if those neurons were turned off seven days after storing the memory, the rats could not recall their fear. The results show that neurons in the PVT-amygdala circuit help to solidify and maintain fear memories, Quirk says.

A second team, led by neuroscientist Bo Li of Cold Spring Harbor Laboratory in New York, used mice to confirm the discovery of the new fear memory circuit. Li and colleagues had previously shown that learning and remembering fear is rooted in the neurons of the central amygdala. Finding that neurons in the PVT region became active and communicated with the central amygdala as mice learned or recalled fear suggested that the region could be important in understanding anxiety disorders.

Li and colleagues wanted to see if a particular brain chemical influences fear memories. Previous research has shown that abnormalities with the protein brain-derived neurotrophic factor, or BDNF, plays a role in post-traumatic stress and other anxiety disorders. Tracking the brain protein in mice showed that it allows neurons in the PVT region to exert control over those in the amygdala, ultimately triggering a response to fear.

Linking how the brain protein and the newly identified fear circuit work together to establish and retrieve fear memories could provide a new target for treatment of post-traumatic stress disorder and other anxiety disorders, Li says. ■

G. QUIRK/UNIV. OF PUERTO RICO SCHOOL OF MEDICINE