How to trigger innate fear response?

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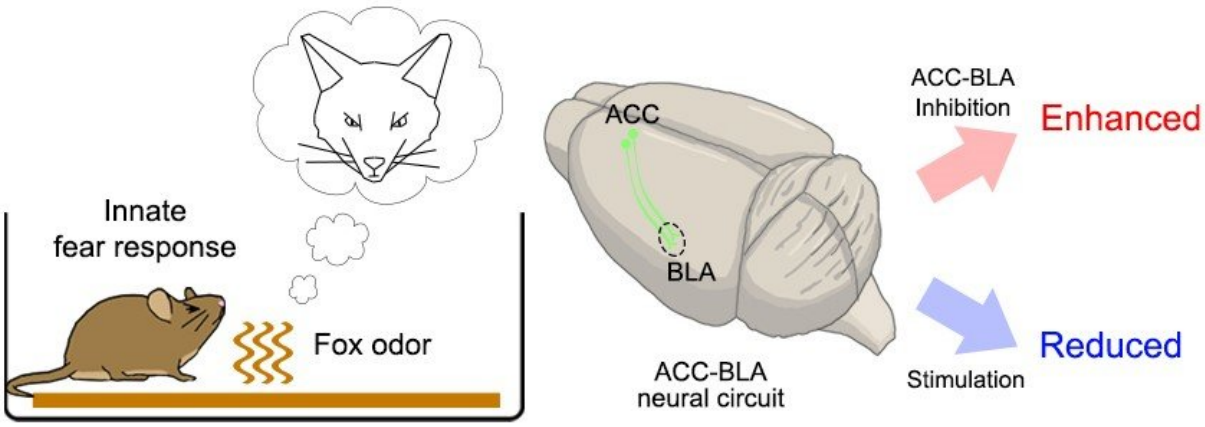

This illustration describes how ACC-BLA circuit controls innate freezing response depending on its activity level. Credit: KAIST

When animals encounter danger, they usually respond to the situation in one of two ways—by freezing or fleeing. How do they make this quick decision in a life-or-death moment?

According to KAIST neuroscientists, there are two types of fear: learned versus innate. The latter is known to be induced without any prior experience and is thus naturally encoded in the brain. A research team under Professor Jin-Hee Han in the Department of Biological Sciences identified the brain circuit responsible for regulating the innate fear response.

The study, which appeared in the July 24 issue of *Nature Communications*, represents a significant step toward understanding how the neural circuits in the prefrontal cortex create behavioral responses to external threats. This also represents a new paradigm in therapeutic development for fear-related mental disorders.

Responses of freezing or fleeing when facing external threats reflect behavioral and physiological changes in an instinctive move to adapt to the new environment for survival. These responses are controlled by the emotional circuit systems of the brain, and the malfunction of this circuit leads to fear-related disorders.

The anterior cingulate cortex (ACC) is a sub-region within the prefrontal cortex comprising a part of the brain circuitry that regulates behavioral and physiological fear responses. This area is capable of high-order processing of the perceived sensory information and conveys 'top-down' information toward the amygdala and brainstem areas, known as the response outlet.

Many studies have already demonstrated that the brain regions in the prefrontal cortex regulate the response against learned threats. However, it has been unknown how innate responses against fear are encoded in the neural circuits in the prefrontal cortex.

Dr. Jinho Jhang, the lead author of the study, explains how the team achieved their key idea. "Many overseas studies have already proved that the prefrontal cortex circuit works to regulate the fear response. However, researchers have paid little attention to the innate response against predators. Professor Han suggested we do research on the instinctive fear response instead of the learned response. We particularly focused on the anterior cingulate region, which has been connected with memory, pain and sympathy, but not the fear response itself. Since we turned in this new direction, we have accumulated some significant

data," said Dr. Jhang.

For this study, Professor Han's team investigated how mice react when exposed to the olfactory stimuli of predators. Based on the results of optogenetic manipulation, neural circuit tracing, and ex vivo slice electrophysiology experiments, the team demonstrated that the anterior cingulate cortex and its projection input to the basolateral amygdala play a role in the inhibitory regulation of innate fear responses to predators' odors in mice.

Professor Han believes these results will extend the understanding of how instinctive fear responses can be encoded in brain circuits. "Our findings will help to develop therapeutic treatments for mental disorders aroused from fear such as panic disorders and post-traumatic stress disorder," said Professor Han.

More information: Jinho Jhang et al, Anterior cingulate cortex and its input to the basolateral amygdala control innate fear response, *Nature Communications* (2018). DOI: 10.1038/s41467-018-05090-y

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