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How the Brain Overcomes Instinctive Fear and Adapts to Threats

Researchers have identified brain mechanisms that help animals suppress instinctive fear responses when threats prove harmless over time.

Using a visual threat model in mice, they found that specific areas of the visual cortex are necessary for learning to override fear, but not for storing the memory. Instead, the ventrolateral geniculate nucleus (vLGN) retains these learning-induced memories, regulating fear suppression. The process is driven by endocannabinoids, which enhance neural activity in vLGN neurons to reduce fear reactions.

These findings challenge traditional views of memory storage and highlight a direct link between cognitive learning and instinctive behaviors. Understanding this mechanism could lead to new treatments for fear-related disorders such as phobias, anxiety, and PTSD.

Key Facts:

- Fear Suppression Memory: The vLGN, not the visual cortex, stores learned fear suppression responses.
- Neural Mechanism: Endocannabinoids regulate vLGN neurons, increasing activity to reduce fear reactions.
- Therapeutic Potential: Targeting vLGN circuits or endocannabinoid pathways could lead to new treatments for anxiety and PTSD.

The research team, led by Dr Sara Mederos and Professor Sonja Hofer, mapped out how the brain learns to suppress responses to perceived threats that prove harmless over time.

"Humans are born with instinctive fear reactions, such as responses to loud noises or fast-approaching objects," explains Dr Mederos, Research Fellow in the Hofer Lab at SWC.

"However, we can override these instinctive responses through experience – like children learning to enjoy fireworks rather than fear their loud bangs. We wanted to understand the brain mechanisms that underlie such forms of learning".

Using an innovative experimental approach, the team studied mice presented with an overhead expanding shadow that mimicked an approaching aerial predator. Initially, the mice sought shelter when encountering this visual threat.

However, with repeated exposure and no actual danger, the mice learned to remain calm instead of escaping, providing researchers with a model to study the suppression of fear responses.

Based on previous work in the Hofer Lab, the team knew that an area of the brain called the ventrolateral geniculate nucleus (vLGN) could suppress fear reactions when active and was able to track knowledge of previous experience of threat.

The vLGN also receives strong input from visual areas in the cerebral cortex, and so the researchers explored whether this neural pathway had a role in learning not to fear a visual threat.

The study revealed two key components in this learning process: (1) specific regions of the visual cortex proved essential for the learning process, and (2) a brain structure called the ventrolateral geniculate nucleus (vLGN) stores these learning-induced memories.

"We found that animals failed to learn to suppress their fear responses when specific cortical visual areas where inactivated. However, once the animals had already learned to stop escaping, the cerebral cortex was no longer necessary," explained Dr

Mederos.

"Our results challenge traditional views about learning and memory," notes Professor Hofer, senior author of the study.

"While the cerebral cortex has long been considered the brain's primary center for learning, memory and behavioral flexibility, we found the subcortical vLGN and not the visual cortex actually stores these crucial memories.

"This neural pathway can provide a link between cognitive neocortical processes and 'hard-wired' brainstem-mediated behaviors, enabling animals to adapt instinctive behaviors."

The researchers also uncovered the cellular and molecular mechanisms behind this process. Learning occurs through increased neural activity in specific vLGN neurons, triggered by the release of endocannabinoids – brain-internal messenger molecules known to regulate mood and memory.

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