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Study sheds light on brain's fear processing center

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Breathing carbon dioxide can trigger panic attacks, but the biological reason for this effect has not been understood. A new study by University of Iowa researchers shows that carbon dioxide increases brain acidity, which in turn activates a brain protein that plays an important role in fear and anxiety behavior.

The study, published in the Nov. 25 issue of the journal *Cell,* offers new possibilities for understanding the biological basis of panic and anxiety disorders in general and may suggest new approaches for treating these conditions.

The researchers focused on a brain protein known as acid-sensing ion channel 1a (ASIC1a). This protein is abundant in the amygdala -- the region deep in the brain that processes fear signals and directs fear behavior. The UI team previously found that blocking or removing ASIC1a reduces innate fear and alters fear memory in mice.

"As long ago as 1918, scientists learned that carbon dioxide triggers abnormal responses in patients with anxiety disorders, but our study provides the first molecular evidence for a mechanism that explains how carbon dioxide can trigger fear and anxiety," said John Wemmie, M.D., Ph.D., associate professor of psychiatry and neurosurgery at the UI Carver College of Medicine and a staff physician and researcher at the Iowa City Veterans Affairs Medical Center. "The findings are a foundation for saying that ASIC proteins in the amygdala might play a key role in sensitivity to carbon dioxide."

In addition to helping explain why breathing carbon dioxide can trigger panic attacks, the study also suggests a new role for the amygdala as a sensor that can detect certain fear signals for itself.

"This is a new finding that the amygdala, which is considered the brain's computer processor for fear, can also function as a sensor for detecting chemical signals -- carbon dioxide and acidity (low pH) -- that are known to trigger panic attacks in susceptible individuals," Wemmie said.

Carbon dioxide inhalation can be deadly at high doses. The study suggests that evolution may have provided humans with a vital ability to detect and respond rapidly to carbon dioxide by placing within the same brain region the ability to detect the threat posed by carbon dioxide and the ability to initiate a "fight or flight" response.

The new study shows that inhaled carbon dioxide increases brain acidity and evokes fear behavior in mice by activating ASIC1a in the amygdala. Fear memory is also enhanced when carbon dioxide activates the protein.

Conversely, the study team, including first author Adam Ziemann, M.D., Ph.D., found that making brain tissue less acidic (raising brain pH) blunted fear behavior produced by carbon dioxide and reduced learned fear.

"It's been suggested that controlling breathing with breath exercises could have anti-anxiety effects," Wemmie said. "Our results make me wonder if some of those breath exercises to control fear and anxiety might be acting by inhibiting the ASIC channels in the amygdala by raising the pH."

Wemmie and his colleagues are now investigating whether ASIC1a abnormalities contribute to panic and anxiety disorder in people or to

carbon dioxide sensitivity in patients with panic disorder.

If ASIC1a plays the same role in people as the studies suggest it does in mice, then drugs that target ASIC channels or strategies that alter brain acidity could hold promise for treating a wide range of panic and anxiety disorders.

Source: University of Iowa (news : web)