Functional connection between hippocampus and cortex modulates anxiety

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A new study demonstrates that cooperation between the hippocampus, best known for its critical role in learning and memory, and a principal downstream cortical target modulates anxiety-related behaviors in mice. The research, published by Cell Press in the January 28th issue of the journal *Neuron*, provides intriguing insight into how anxiety is processed in the brain and may help to explain what governs anxiety-related behaviors.

Recent research has linked a specific region of the hippocampus, called the ventral hippocampus (vHPC), with anxiety-related behaviors. "While we have known for some time that the vHPC plays a key role in anxiety-like behaviors in rodents, how it does so was unclear," explains senior study author, Dr. Joshua A. Gordon from the Department of Psychiatry at Columbia University. "We wondered whether it might influence anxiety by interacting with other brain regions thought to be important."

Dr. Gordon and colleagues tested this hypothesis by recording electrical activity from the vHPC and the medial prefrontal cortex (mPFC) in mice as they explored different environments, some of which were known to elicit anxiety. The mPFC was of interest because it was previously shown to play an important role in anxiety and it receives direct input from the vHPC. The researchers looked for a synchronization of brain activity between the brain regions because this is a sign of information transfer or, to put it more simply, that one brain region is talking and the other is listening.

As expected given the fact that they are anatomically connected, brain activity within the vHPC and mPFC were relatively closely synchronized in all environments that the mice explored. Exposure to environments known to generate anxiety increased this synchronization. Specifically, brain activity in the theta-frequency (4-12 Hz) range was affected by anxiety, consistent with previous reports suggesting that theta-frequency synchrony typically mediates communication between the hippocampus and other brain regions. Along with the increase in synchrony, there was also an overall increase in theta-frequency activity in the mPFC that appeared to be involved in the inhibition of exploratory behavior, an anxiety-related response in mice. Interestingly, mice genetically engineered to exhibit increased anxiety exhibited larger theta increases than normal mice.

The results are the first concrete demonstration that the vHPC and the mPFC cooperate during anxiety. "Our findings suggest that the vHPC sends the mPFC large-scale information about the emotional salience of the environment, which allows the mPFC to recognize the environment as threatening," says Dr. Gordon. "The mPFC may in turn modulate other brain areas, such as the amygdala, to produce appropriate defensive and anxiety-related behaviors." The authors point out that additional studies are needed to further explore the significance of the vHPC-mPFC connection and to determine whether similar circuits are operating in humans with anxiety disorders.

More information: Adhikari et al.: "Synchronized Activity between the Ventral Hippocampus and the Medial Prefrontal Cortex during Anxiety." Publishing in Neuron 65, 257-269, January 28, 2010. DOI:10.1016/j.neuron.2009.12.002

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