NEUROSCIENCE

Astrocyte activation induces anxiolytic behavior in mice

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While new research continues to add evidence for the role of astrocytes in brain functions and behaviors, many questions remain about their capacity to influence affective behaviors. By showing that hippocampal astrocyte activation induces anxiolytic effects and increases exploratory drive in mice, a new study might open up new avenues for treating anxiety disorders.

In the brain, astrocytes intimately interact with neuronal synapses to form the 'tripartite synapse'. Astrocytes regulate synapse formation and actively control synaptic transmission via the release of gliotransmitters. Astrocyte dysfunction has been implicated in several neurodegenerative diseases, and increasing evidence indicates astrocytes might also contribute to psychiatric diseases. In this new study, Cho, Noh and colleagues explored the role of astrocytes located in the hippocampus – a brain region associated with anxiety – in anxiety-like behaviors.

First, the team developed a mouse model expressing calcium indicator GCaMP6s specifically in astrocytes. Analysis of Ca^{2+} activity in head-fixed awake hGFAP-GCaMP6s mice exposed to virtual reality (VR) environment emulating either a closed or an open arm of an elevated plus maze (EPM), revealed an intracellular Ca^{2+} increase in hippocampal astrocytes when mice were exploring the open center of the VR. "These results imply that hippocampal astrocytes are activated upon exposure to innately visual-based anxiogenic environment, and suggest that the Ca^{2+} activity of hippocampal astrocytes discerns or reflects anxiety state," explain the investigators in their report.

Next, the researchers used an optogenetic approach to explore whether hippocampal astrocyte activation directly influences anxiety-like behavior. In the EPM, after light stimulation in the hippocampus, transgenic mice expressing channelrhodopsin 2 (ChR2) in astrocytes spent more in the open arm and less time in the closed arms compared to control mice not expressing ChR2. Similarly, in the open-field test, hippocampal astrocyte activation led to a dramatic increase in exploration, indicating that hippocampal astrocyte activity modulates anxiety-related behavior.

Finally, further experiments revealed that astrocyte activation induced anxiolytic behavior via ATP release. "We reveal an unexpected role of hippocampal astrocytes that respond to anxiogenic environment and modulate mice anxiety-like behavior by regulating synaptic activity of granule cells via ATP release. These data may offer a strategy to treat anxiety disorders by targeting hippocampal astrocytes," conclude the investigators.

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