MedicalXpress

Blame it on the astrocytes

July 11 2014

In the brains of all vertebrates, information is transmitted through synapses, a mechanism that allows an electric or chemical signal to be passed from one brain cell to another. Chemical synapses, which are the most abundant type of synapse, can be either excitatory or inhibitory. Synapse formation is crucial for learning, memory, perception and cognition, and the balance between excitatory and inhibitory synapses critical for brain function. For instance, every time we learn something, the new information is transformed into memory through synaptic plasticity, a process in which synapses are strengthened and become more responsive to different stimuli or environmental cues. Synapses may change their shape or function in a matter of seconds or over an entire lifetime. In humans, a number of disorders are associated with dysfunctional synapses, including autism, epilepsy, substance abuse and depression.

Astrocytes, named for their star-like shape, are ubiquitous brain cells known for regulating excitatory synapse formation through cells. Recent studies have shown that astrocytes also play a role in forming inhibitory synapses, but the key players and underlying mechanisms have remained unknown until now.

A new study just published in the journal *Glia* and available online on July 11th, details the newly discovered mechanism by which astrocytes are involved in inhibitory synapse formation and presents strong evidence that Transforming Growth Factor Beta 1 (TGF β1), a protein produced by many cell types (including astrocytes) is a key player in this process. The team led by Flávia Gomes of the Rio de Janeiro Institute of

Biomedical Sciences at the Federal University of Rio de Janeiro investigated the process in both mouse and human tissues, first in test tubes, then in living brain cells.

Previous evidence has shown that TGF β1, a molecule associated with essential functions in nervous system development and repair, modulates other components responsible for normal brain function. In this study, the authors were able to show that TGF β1 triggers N-methyl-D-aspartate receptor (NMDA), a molecule controlling memory formation and maintenance through synaptic plasticity. In the study, the group also shows that TGF β1-induction of inhibitory synapses depends on activation of another molecule - Ca2+/calmodulin-dependent protein kinase II (CaMK2)-, which works as a mediator for learning and memory. "Our study is the first to associate this complex pathway of molecules, of which TGF β1 seems to be a key player, to astrocytes' ability to modulate inhibitory synapses", says Flávia Gomes.

The idea that the balance between excitatory and inhibitory inputs depends on astrocyte signals gains strong support with this new study and suggests a pivotal role for astrocytes in the development of neurological disorders involving impaired inhibitory synapse transmission. Knowing the players and mechanisms underlying inhibitory synapses may improve our understanding of synaptic plasticity and cognitive processes and may help develop new drugs for treating these diseases.

More information: "Astrocyte Transforming Growth Factor Beta 1 Promotes Inhibitory Synapse Formation Via Cam Kinase II Signaling" *Glia*, onlinelibrary.wiley.com/journa … 1002/(ISSN)1098-1136

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