Dopamine-evoked synaptic regulation in the brain reward system requires astrocyte activity

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Dopaminergic signaling in the nucleus accumbens (NAc) plays key roles in neuronal network activity underlying reward and drug seeking behaviors[1-3]. Accumulating evidence indicates that astrocytes play a role in learning, memory and neural information processing by actively modulating neuronal activity and synaptic function[4,5]. Astrocytes respond to synaptically-released neurotransmitters with intracellular calcium elevations and the release of gliotransmitters that modulate synaptic transmission and impact animal behavior. While dopaminergic signaling system has been mainly studied in neurons, the involvement of astrocytes in dopaminergic signaling in this brain area remains largely unknown. We have investigated astrocytic responsiveness to dopamine and the consequent regulation of synaptic transmission in the NAc core.

Methods: We used combined electrophysiological and calcium imaging techniques in brain slices. We used exogenous application of dopamine or selective optogenetic stimulation of dopaminergic axons to investigate astrocytic responsiveness to dopamine. To investigate the consequences of astrocytes activation on synaptic transmission we performed electrophysiological recordings of glutamatergic synaptic transmission and activated astrocytes with exogenous dopamine application, selective optogenetic stimulation of dopaminergic axons, or by activating Designer Receptors Exclusively Activated by Designer Drugs (DREADDs) specifically expressed in astrocytes.

Results: We found that astrocytes responded to exogenous (dopamine application) and endogenous (optogenetic activation of dopaminergic axons) dopamine with intracellular calcium elevations. These dopamine-induced calcium elevations in astrocytes were associated with a depression of excitatory synaptic transmission through activation of adenosine A_1 receptors. Furthermore, specific activation of astrocytes with DREADDs resulted in a depression of synaptic transmission that mimicked the dopamine-mediated synaptic depression.

Discussion: Present results indicate that astrocytes in the NAc core are involved in dopaminergic signaling by responding to dopamine and mediating a dopamine-induced synaptic depression. These results advance our current knowledge of the astrocyte involvement in dopaminergic signaling in the NAc revealing their potential role as targets for treatment of disorders of motivation such as addiction.

References

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