Division of Medical Sciences

Seminar Series 2024 – 2025

Astrocytic Ensheathment of Glutamate Synapses in the Accumbens is Highly Variable

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The concept of the tripartite synapse poses that pre- and postsynaptic structures in excitatory axospinous contacts are closely apposed by a third astrocytic element participating in communication and plasticity with both sides of the junction. Since the pioneering reconstructions of the hippocampus by Kristen Harris, it has been known that over 40% of excitatory synapses on spines in that region are without astrocytic contacts, and those that are contacted are covered on only 40% of the available synaptic surface. Given that astrocytes clear extracellular glutamate, these observations have profound implications for understanding how excitatory synapses are regulated and therefore how they may operate as independent computational elements. Despite such importance, these parameters have not been investigated within the striatal complex where cortical afferents critically regulate goal-directed behavior. We have examined astrocytic ensheathment of axospinous synapses in the nucleus accumbens core, a region for which glutamate homeostasis vitally contributes to and is shaped by drugs of abuse. We have investigated naïve rats and mice using electron microscopy and 3D reconstruction of excitatory-type axospinous synapses: over 300 from rats and over 100 from mice. Roughly one-third of these synapses exhibited no astrocytic contact. Of the synapses showing some ensheathment, only one-third of the available synaptic surface was contacted on average. The findings were consistent across the two species and comparable to those reported for the hippocampus. A second pilot study was done in collaboration with Dr. Yan Dong at the University of Pittsburgh to begin investigating ultrastructural changes in response to chronic cocaine. Four rats were examined, two each self-administering saline or cocaine for 5 days. Reconstruction of 72 synapses from saline animals and 77 synapses from cocaine rats showed no significant differences in any morphological measure or the proportion of astrocytic contact with synapses. For both studies, marked variation in most dependent measures was seen within and across animals regardless of treatment status. Hence, much greater sample sizes are needed before any significant structural impact of cocaine can be uncovered. Understanding how astrocytes regulate glutamate homeostasis in healthy and drug-exposed animals is essential for developing novel treatments for substance use disorder.

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