

S02-3 **Astrocyte-to-astrocyte and astrocyte-to-neuron communications mediated by extracellular ATP**

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Astrocytes could communicate adjacent glial cells, neurons and vascular systems by releasing so-called gliotransmitters. Extracellular ATP has a central role as a gliotransmitter in the CNS. Astrocytes release ATP in response to neuronal excitations, which was followed by a dynamic modulation of synaptic transmission. In addition, astrocytes show a constitutive ATP release, resulting in a tonic regulation of neuronal activities including upregulation of neurotransmitter receptors. Firstly, we review the latest findings concerning the gliotransmitter-mediated regulation of brain functions. Next, we show a mechanism(s) underlying release of gliotransmitter ATP from astrocytes. There are several reports in that astrocytes release ATP in response to various stimuli. However, the mechanisms for the release are debatable. Astrocytes release ATP via Cl⁻ channels, maxi anion channels, connexin hemi-channels, P2X7 receptors and exocytosis. Astrocytes seem to have multiple pathways for the release of ATP. Among them, we focused on exocytosis of ATP. Astrocytes could release ATP in a Ca²⁺-dependent mechanism. We also found ATP-containing vesicles inside of astrocytes, suggesting that astrocytes release ATP by a mechanism of exocytosis. In addition to diffusible secretion by opening of ATP-permeable channels, astrocytes have a mechanism of exocytosis, by which astrocytes release ATP more positively and regularly. So-called “tripartite synapse” hypothesis has been proposed, and astrocyte could function as a peri-synapse. In this regard, the finding that astrocytes could release ATP in an exocytotic mechanism(s) is very important, and would contribute to elucidate the synaptic transmissions in the CNS.