SPP 1172

Communication between cortical neurons and astrocytes by extracellular ATP and glutamate



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Speaker:

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Project discription:

It has repeatedly been shown that astrocytes release glutamate in response to ATP application. The following experiments are designed to investigate the morphological basis and the functional consequences of this release: 1. Interaction between P2Y and NMDA receptors in pyramidal neurons of the rat cortex. (A) In slices of the rat prefrontal cortex, astrocytic glutamate may activate metabotropic glutamate receptors (mGluR) of layer V pyramidal neurons and thereby increase the conductance of neighboring NMDA receptor-channels. It will be elucidated by the patch-clamp method, which group/type of mGluR is involved in this effect. (B) Experiments made in brain slices will be replicated in mixed astrocytic/neuronal cultures of the rat cerebral cortex to find out whether the mGluR-NMDA receptor interaction occurs in pyramidal neurons only. In acutely dissociated pyramidal neurons and in the absence of astrocytes a receptor-interaction will probably not take place. (C) Ca2+-imaging in the mixed astrocytic/neuronal cultures will confirm the above findings and help to localize the site of the mGluR-NMDA receptor interaction to cell bodies or neuronal processes. 2. Cellular and subcellular localization of P2Y receptors at astrocytes. We will search by confocal laser scanning microscopy and electron microscopy in conjunction with immunohistochemical methods for the pre- and/or postsynaptic expression of P2Yimmunopositivity at neurons and astrocytes in the prefrontal cortex. 3. ATP-induced release of glutamate from astrocytes. (A) HPLC determinations will help to identify the P2Y receptor-type (P2Y1, P2Y2) involved in the release of glutamate by ATP from cell cultures enriched in astrocytes. (B) Microdialysis measurements from the prefrontal cortex of freely moving rats will be used to clarify whether glutamate is released from neurons or astrocytes.

Quelle:

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