MS02-5 **Astrocytes as a potential target for antidepressants**

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Astrocytes, by releasing gliotransmitter ATP, regulate synaptic transmissions. Thus, astrocytic functions could be involved in brain diseases, but little is known about effects of psychotropic drugs on glial cells. Antidepressants are believed to inhibit uptake of monoamines and reveal their therapeutic actions. Recent accumulating evidence show that decrease or dysfunction of brain-derived neurotrophic factor (BDNF) is a key event in pathology of depression, and antidepressants could upregulate BDNF in neurons. However, there is no report about whether antidepressants affect astrocytic BDNF formation. Here we show effects of antidepressants on BDNF expression in astrocytes. Stimulation of hippocampal primary astrocytes with antidepressants dramatically increased both mRNAs and proteins of BDNF. Among antidepressants tested, fluoxetine showed the most potent effects. The upregulation by fluoxetine was inhibited by the P2Y1 receptor antagonist or ATP-degrading enzyme apyrase, suggesting that fluoxetine facilitates astrocytic gliotransmission, i.e., ATP/P2Y1 receptor system. In fact, activation of P2Y1 receptors in astrocytes resulted in upregulation of BDNF. Furthermore, we found that fluoxetine inhibited ecto-nucleotids, which was followed by an increase in extra-astrocytic ATP concentration. Taken together, we concluded that antidepressants could upregulate BDNF by facilitating ATP/P2 receptors in astrocytes and, therefore, astrocytes could be a therapeutic target for antidepressants.