RESEARCH ARTICLE

The A1 Adenosine Receptor as a New Player in Microglia Physiology

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The purinergic system is highly involved in the regulation of microglial physiological processes. In addition to the accepted roles for the $P_2X_{4,7}$ and P_2Y_{12} receptors activated by adenosine triphosphate (ATP) and adenosine diphosphate, respectively, recent evidence suggests a role for the adenosine $A2_A$ receptor in microglial cytoskeletal rearrangements. However, the expression and function of adenosine A1 receptor (A1AR) in microglia is still unclear. Several reports have demonstrated possible expression of A1AR in microglia, but a new study has refuted such evidence. In this study, we investigated the presence and function of A1AR in microglia using biomolecular techniques, live microscopy, live calcium imaging, and *in vivo* electrophysiological approaches. The aim of this study was to clarify the expression of A1AR in microglia and to highlight its possible roles. We found that microglia express A1AR and that it is highly upregulated upon ATP treatment. Moreover, we observed that selective stimulation of A1AR inhibits the morphological activation of microglia, possibly by suppressing the Ca^{2+} influx induced by ATP treatment. Finally, we recorded the spontaneous and evoked activity of spinal nociceptive-specific neuron before and after application of resting or ATP-treated microglia, with or without preincubation with a selective A1AR agonist. We found that the microglial cells, pretreated with the A1AR agonist, exhibit lower capability to facilitate the nociceptive neurons, as compared with the cells treated with ATP alone.

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