Blockade of Adenosine A$_{2A}$ Receptor Attenuates AngII-induced ROS Production and Impairment of Endothelium-dependent Vessel Relaxation in Mouse Aortas

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The endothelium expresses abundantly an adenosine A$_{2A}$ receptor (A$_{2A}$R) which plays important roles in the regulation of vascular function. The endothelium expresses also the AT1-type receptor for angiotensin II (AngII) which has been found to activate a reactive oxygen species (ROS) generating NADPH oxidase and cause oxidative damage to the endothelium. However little is known about the role of A$_{2A}$R in AngII-induced endothelial ROS production. In this study, we investigated the effect of A$_{2A}$R blockade on AngII-induced ROS production and endothelium function using freshly isolated aortas from CD1 mice at 10-12 weeks of age. Compared to vessels treated with vehicle, acute AngII (200 nM for 45 min) treatment significantly increased the ROS production in the vessel wall as detected by DHE fluorescence and this was accompanied by an increased ERK1/2 phosphorylation. These AngII effects were inhibited back to the control levels in the presence of a specific A$_{2A}$R antagonist, SCH58261 (100 nM). Compared to control vessels, treatment with AngII severely compromised the endothelium-dependent vessel relaxation to acetylcholine as assessed by an organ bath. Addition of SCH58261 (100 nM) or tiron (20 mM, a specific cell membrane permeable superoxide scavenger) during AngII stimulation protected the endothelium from AngII damage and preserved endothelium-dependent vessel relaxation to acetylcholine. The endothelium-dependence of the relaxation to acetylcholine was confirmed by mechanical denudation of the endothelium. In conclusion, blockade of A$_{2A}$R protects the endothelium from acute AngII-induced oxidative stress, ERK1/2 phosphorylation and endothelium dysfunction.