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Adenosine modulation of signaling at the tripartite synapse: Implications for Epilepsy

A denosine is an endogenous anti-epileptic substance, known for its ability to inhibit excitatory synaptic transmission. I will focus on recent work by our group aiming to elucidate how high affinity A1 (A_1R) and A_{2A} ($A_{2A}R$) adenosine receptors affect not only excitatory but also inhibitory transmission at the hippocampus. A2ARs can directly interfere with the life-span of GABA at synapses, since GABA transport is facilitated by $A_{2A}R$ s in nerve endings and astrocytes, where A_1R and $A_{2A}R$ act as tetramers to fine tune GABA uptake. A1R inhibits the function of GABA $_A$ receptors localized at perisynaptic/extrasynaptic compartments in excitatory and a subset of inhibitory neurons, being involved in the control of persistent tonic GABAergic responses. $A_{2A}R$ s influence the GABAergic input to a subset of inhibitory neurons and promote synchronous pyramidal cell firing in hyperexcitable conditions. In addition, $A_{2A}R$ s enhance extrasynaptic AMPA receptor mediated responses, allow the sustained recruitment of calcium-permeable AMPA receptors after ischemia, leading to a long-lasting facilitation of excitatory synaptic transmission and trigger neurotrophic factor actions upon synaptic plasticity. These actions of adenosine contribute to fine-tune neuronal activity and to set the stage for plasticity, eventually influencing seizure-induced aberrant plasticity.

Biography

Ana Maria Sebastiao has completed his PhD in 1987 from the Gulbenkian Institute of Science and the New University of Lisbon. She is the Director of the Institute of Pharmacology and Neuroscience, Medical School, University of Lisbon, and of the Mind-Brain College of the University of Lisbon, Portugal. She has published more than full 140 papers quoted more than 4600 times, and has been serving as an Editorial Board Member of several journals. She also served as President of the Portuguese Neuroscience and Portuguese Pharmacological Societies as well as in the Executive Council of the Federation of European Pharmacological Societies.

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