EFFECT OF NUCLEOSIDE TRANSPORT INHIBITION ON THE INTERSTITIAL ADENOSINE CONCENTRATION IN THE MICROENVIRONMENT OF A_1 ADENOSINE RECEPTORS IN EU- AND HYPERTHYROID GUINEA PIG ATRIA

Dénes Karsai

In our studies, two methods were used to characterize and compare the change in $[Ado]_{ISF}$ elicited by NT blockade: an algebraic calculation based on the relationship expressed in the Langmuir-Hill equation, and a regression analysis by fitting a concentration determining equation derived from the Langmuir-Hill equation („receptorial responsiveness method": RRM). On the basis of our results, the RRM enables the characterization of a change in concentration of an agonist or a modulator in the microenvironment of its receptor, when the Langmuir-Hill equation cannot be used due to degradability of the given agent. The impact of this method stems from the fact that concentration of degradable agents is difficult to assess in the compartment containing the receptors of the agents. By means of the RRM, changes in concentration of degradable agents practically immeasurable directly can be characterized by concentrations of stable agents, which have signal-transduction similar to degradable agents in question.

With the help of the index provided by the RRM, changes in concentration of degradable agents become comparable even between tissues with different enzyme and transporter activities. It is well-known that several enzyme and carrier activities are modified in the hyperthyroid heart. Since these alterations hardly affect elimination of CPA, a relatively stable compound in asanguineous atrial tissue, the change in $[Ado]_{ISF}$ accompanying NT blockade can be reliably characterized by the equieffective concentration of CPA computed by the RRM (c_x). Our results show that NT inhibition causes an increase in c_x approximately 2-2.5 fold greater in hyperthyroid atria than in euthyroid ones, indicating a greater increase in $[Ado]_{ISF}$ elicited by NT blockade in hyperthyroid atria. It can be concluded that hyperthyroidism does not alter the physiological direction of NT; moreover it does enhance NT directed to the cell interior as compared to the euthyroid condition.