

## **Effects of blockade of hyperpolarization-activated ion currents (I<sub>h</sub>) on autonomic control of the heart in rats: Age-related peculiarities**

Zefirov T., Ziyatdinova N., Zefirov A.  
*Kazan Federal University, 420008, Kremlevskaya 18, Kazan, Russia*

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### **Abstract**

In our experiments, we studied the effects of intravenous introduction of ZD7288, a selective blocker of the currents activated by hyperpolarization (I<sub>h</sub>), on the cardiac activity of 1- and 3-week-old and young adult (20-week-old) rats. Introduction of the blocker caused a dose-dependent decrease in the heart rate (HR) in all age groups. A maximum and a minimum expression of bradycardia were observed in 1- and 3-week-old rats, respectively. Stimulation of the n. vagus against the background of bradycardia that developed after the blockade of I<sub>h</sub> led to a further drop in the HR. In this case, the expression of the effect of stimulation of the n. vagus depended on the dose of the introduced blocker. The blockade of I<sub>h</sub> influenced the cardiac reaction to introduction of an agonist of  $\beta$ -adrenoreceptors, isoproterenol, in rats of early age and young adult rats, but not in 3-week-old rats. Therefore, the blockade of I<sub>h</sub> changes the reaction of the heart on sympathetic and parasympathetic regulatory influences, and the expression of these changes significantly depends on the animal's age. This allows us to conclude that not only the pacemaker activity of cardiomyocytes per se but also autonomic modulation of the cardiac activity demonstrate a significant dependence on the function of hyperpolarization-activated ionic channels; this function is characterized by substantial age-related peculiarities. © 2003 Plenum Publishing Corporation.

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### **Keywords**

Autonomic control, Cardiac activity, Hyperpolarization-activated ion currents, n. vagus, Ontogenesis