PHYSIOLOGY

Effect of Vagal Stimulation on Cardiac Rhythm in Rats under Blockade of β-Adrenoreceptors by Obsidan

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Obsidan induced age-dependent bradycardia in intact rats and in rats with chemical sympathetic denervation. Subsequent vagal stimulation produced further decrease in heart rate. Administration of atropine to obsidan-treated rats increased heart rate.

Key Words: *rat; vagus; chemical sympathetic denervation; cardiac rhythm; obsidan*

The degree of postvagotomy tachycardia varies in different species [7]. In small rodents the vagal tone is the lowest [5]. Inhibition of cardiotropic adrenergic influences produces only minor changes in heart rate in humans [9] and dogs [10]. The release of norepinephrine is regulated by adrenoreceptors of various types. Down-regulation of this release is mediated by α-adrenoreceptors, while up-regulation is activated by stimulation of β-adrenoreceptors [6]. However, the direct effect of catecholamines on postsynaptic β-adrenoreceptors in the pacemakers cannot be ruled out [8]. Different effects of vagotomy on the dynamics of variational pulsogram were revealed in rats of different ages subjected to sympathetic denervation (SD) [2]. At the same time, electrical stimulation of the vagi resulted in profound tachycardia both in intact and SD-animals [3].

Our aim was to study the dynamics of cardiac variational pulsogram parameters in rats of different ages with SD produced by pharmacological means during vagal stimulation after blockade of cardiac β-adrenoreceptors by obsidan.

MATERIALS AND METHODS

The study was carried out on 4, 6, 8, and 20-week-old random-bred albino rats. The test group consisted of SD rats. Chemical SD was performed in neonatal rats by daily subcutaneous injections of guanethidine sulfate (10 ml/kg body weight) during a 28-day period. The control group consisted of rats of the same age which were kept under identical conditions.

Both the vagi and the right femoral vein were dissected in narcotized rats (urethane 800 mg/kg) under a microscope. Obsidan (0.8 mg/kg) and atropine (0.6 mg/kg) were injected intravenously.

Vagal electrical stimulation was performed with 5-V pulses generated by an ESL-2 stimulator. Repetition rate, duration, and delay of the pulses were chosen individually for every rat.

The signals from an EKSP-02 electrocardiograph were fed into a C1-83 oscilloscope via an original interface and into a microcomputer via an F707732 digitizer. This computer was also used to control the set-up.

The ECG was recorded and processed on-line [1]. The original software calculated 13 parameters of the variational pulsogram from the arrays of the cardiointervals [4]. Six parameters were analyzed statistically: mean cardiointerval (Xmean), mode, amplitude of the mode, variation range (ΔX), standard deviation (δ), and tension index (TI).

RESULTS

Intravenous injection of obsidan produced pronounced bradycardia in all age groups of intact and SD-ani-

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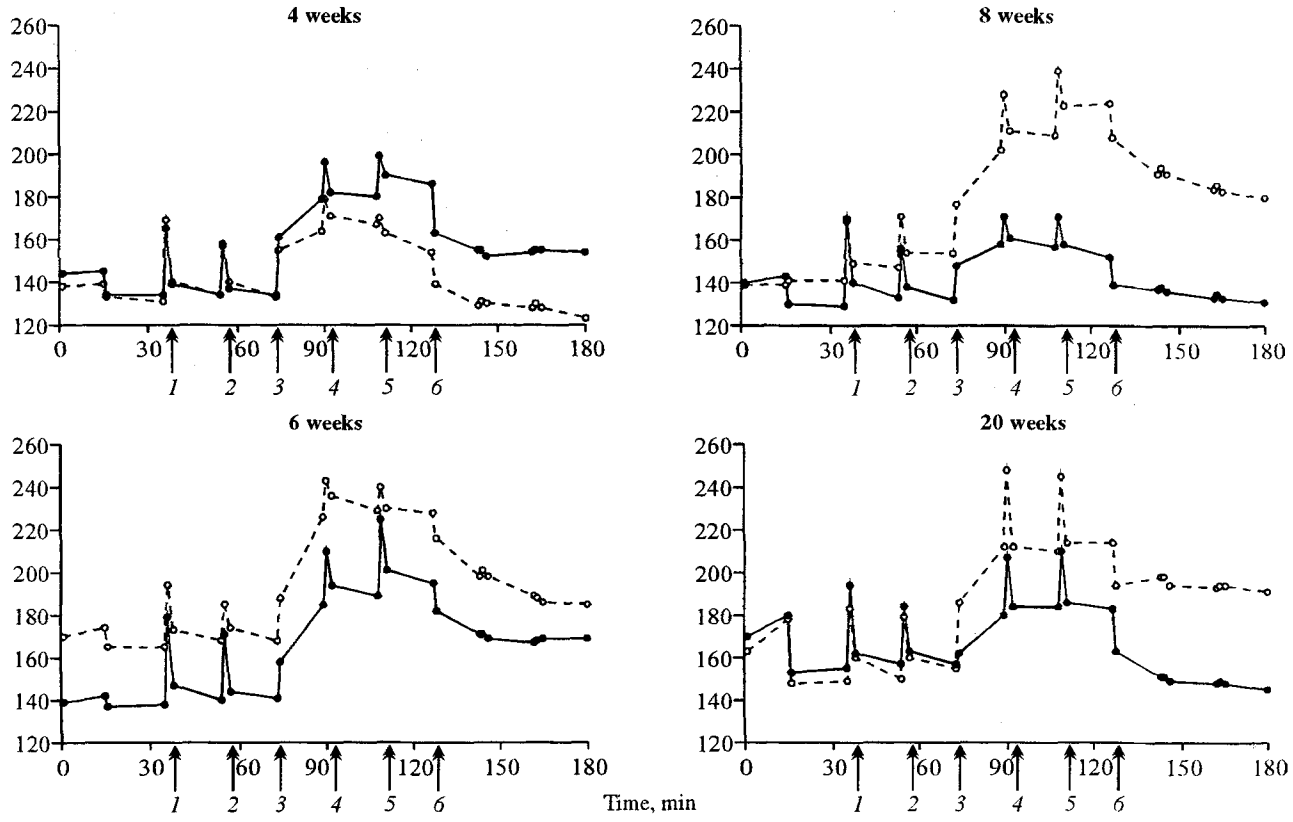

Fig. 1. Dynamics of mean cardiointerval (msec) in intact (dashed line) and sympathetically denervated (solid line) rats of different ages. Stimulation of right (*1*, *4*) and left (*2*, *5*) vagus; intravenous administration of obsidan (*3*) and atropine (*6*).

mals, but statistical significance of the changes in the parameters of variational pulsogram was different in control and test rats. In 4-week-old neonatal SD-rats, obsidan induced a significant increase of Xmean during the first minute postinjection ($p<0.05$). By contrast, statistically insignificant increase of Xmean by 23% was observed in the intact rats of the same age even 15 min postinjection (Fig. 1). In neonatal SD-rats obsidan produced a significant ($p<0.05$) short-term increase of δ, ΔX, and mode, and decreased mode amplitude and TI ($p<0.001$). Then this parameter rapidly normalized. Blockade of β-adrenoreceptors in 6-week-old rats produced gradual statistically significant bradycardia. Cardiac automatism virtually did not change in intact rats, while in 6-week-old neonatal SD-rats marked disturbances were observed in cardiac automatism with subsequent restoration of d and DX. In 8-week-old intact and SD-rats obsidan induced statistically significant bradycardia within the first minute postinjection ($p<0.001$, Fig. 1). In 8-week-old SD-rats the increase in Xmean was accompanied by significant changes in other parameters of the variational pulsogram, while the corresponding changes were small in intact rats of the same age.

In 20-week-old intact rats obsidan induced a significant increase in Xmean within the first minute postinjection ($p<0.001$). In adult SD-rats the increase of Xmean became statistically significant ($p<0.05$) only 15 min after injection of obsidan (Fig. 1).

In intact rats the degree of bradycardia induced by obsidan blockade of β-adrenoreceptors increased with age. By contrast, in SD-rats the statistical significance of bradycardia caused by intravenous administration of obsidan decreased with age. Comparison of the obsidan-induced changes in cardiac rhythm in intact and SD-rats at various stages of postnatal development suggests an age-related increase in sympathetic influences on cardiac rhythm.

Electrical stimulation of the vagi nerves against the background of obsidan produced bradycardia in all rats of intact and denervated groups, statistical significance of bradycardia being increased with age. In addition, bradycardia was accompanied by pronounced disturbances in cardiac automatism and was characterized by predominance of parasympathetic influences.

Injection of atropine 45 min after obsidan caused tachycardia both in intact and SD-rat of all ages (Fig. 1). Statistical significance of tachycardia produced by atropine under the effect of obsidan was higher in SD-rats. The dynamics of ΔX, mode amplitude and TI reflects the prevalence of parasympathetic influences.

Thus, obsidan produces pronounced bradycardia, but did not block the inhibition of cardiac activity caused by vagal electrical stimulation. Pharmacological SD did not modify the reaction to obsidan. Blockade of M-cholinoreceptors by atropine under the effect of obsidan induced tachycardia. Our findings are consistent with the data on important role of β_2-adrenoreceptors in cardiac rhythm adjustment in postnatal rats [11].

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