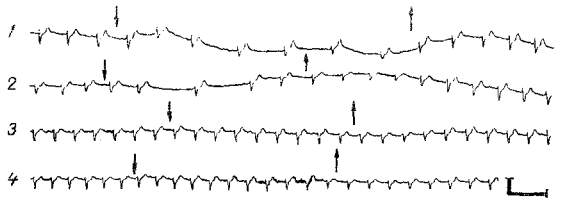

Fig. 2. Changes in cardiac rhythm as shown by ECG (lead V_2) during self-stimulation of abdominal receptors before (1) and 5 (2), 20 (3), and 40 min (4) after injection of atropine. Arrows indicate beginning and end of self-stimulation of abdominal receptors. Calibration: 1 mV, 1 sec.

compressed and distended their abdomen with the aid of the diaphragm and abdominal muscles. As a result of these exercises, after only 1 week both volunteers were able to reduce their heart rate appreciably without any particular effect (Fig. 2). Injections of atropine into the volunteers in a dose of 1 mg subcutaneously completely prevented this "voluntary" control of their heart beat. The facts described above thus confirmed once again the validity of the classical view that purely voluntary control of the cardiac rhythm is impossible, but at the same time, they showed how it can be successfully imitated over a wide range of frequencies. This procedure can evidently be used in clinical practice to explain and correct types of cardiac arhythmia, and also to produce conditioned-reflex inhibition of cardiac activity.

LITERATURE CITED

1. O. V. Bogdanov, A. A. Smetankin, Yu. S. Inin, and Yu. V. Khakhan, Fiziol. Cheloveka, 9, No. 5, 753 (1983).
2. V. V. Orlov and A. N. Timofeev, The Regional and Systemic Circulation [in Russian], Leningrad (1978), pp. 166-177.
3. V. M. Pokrovskii V. G. Abushkevich, A. I. Dashkovskii, and S. V. Shapiro, Dokl. Akad. Nauk SSSR, 283, No. 3, 738 (1985).
4. M. A. Bouchard and J. La Belle, Biofeedback Self Regul., 7, No. 2, 121 (1982).
5. J. P. Hatch and R. J. Gatchel, Biofeedback Self Regul., 6, No. 2, 139 (1982).
6. D. W. Johnston, C. R. Lo, G. V. Marie, and J. Van Jones, Acta Med. Scand., Suppl. 660, 238 (1982).
7. T. Kadil, Z. Bohdadecky, and J. Simek, Internationaler Wissenschaftlicher Kolloquium 30: Vorträge, No. 2, Ilmenau (1985), pp. 197-199.
8. J. L. Reeves and D. Shapiro, Biofeedback Self Regul., 8, No. 1, 87 (1983).
9. D. A. Williamson, M. P. Jarell, J. E. Monguillot, and P. Hutchinson, Biofeedback Self Regul., 8, No. 1, 39 (1983).

TEMPERATURE SENSITIVITY OF AFFERENT RECEPTORS OF THE ISOLATED RABBIT BRAIN

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KEY WORDS: heart; afferent receptors; temperature sensitivity.

Abundant experimental evidence has been obtained by the study of physiological properties of cardiac receptors connected by afferent fibers with the CNS. Most of these receptors are atrial and ventricular mechanoreceptors, but pericardial and epicardial receptors also have been found. The adequate stimulation for activation of the afferent receptors of the heart is stretching of its chambers. Epicardial receptors also are stimulated by some chemicals (acetylcholine, veratrine, etc.) and they can respond to metabolic changes in the body [6, 8]. Previously, in experiments on cats in situ, the authors found that afferent receptor zones reponding to changes in temperature of the inflowing blood can exist in principle in the heart [1, 2]. It was shown that besides the well-known myogenic responses, a rise (or

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TABLE 1. Changes in Positive Chronotropic Effect (in %) on Irrigation of Epicardial Surface of Isolated Rabbit Heart with Warm Krebs–Henseleit Solution after Intracoronary Injection of Ganglion Blocker Arfonad (10 mg/ml)

Experimental conditions	Number of tests	Chronotropic effect, %
Control	69	20,6 (6—41)
After injection of Arfonal		
2—3 min	23	12,8* (0—23)
5—10 min	23	21,9** (5—40)

Legend. Arithmetic mean values and limits of variations shown. *$p < 0.01$, **$p < 0.05$ compared with control.

fall) of temperature evokes neurogenic chronotropic effects, which may probably arise through central or intracardiac reflexes. This latter suggestion was based on the fact that, as was shown previously [3, 5, 9], even after complete denervation the heart still remains amenable to self-regulation on account of activation of the afferent component of the intracardiac reflex. Just as in the case of central reflexes, the adequate excitatory stimulus in this case is stretching. Besides this, it may also be that the afferent component of the intracardiac reflex can be evoked by a change in temperature of different parts of the endocardium and epicardium.

The aim of this investigation was to study the temperature sensitivity of afferent receptors of the isolated rabbit heart before and after blockade of the intracardiac reflexes by means of a ganglion blocker.

EXPERIMENTAL METHOD

Rabbits were anesthetized with pentobarbital (40 mg/kg, intravenously), thoracotomy performed, and the heart and adjacent vessels isolated. The isolated heart, after removal of the pericardium, was perfused by Langendorff's method with Krebs–Henseleit solution (NaCl – 118 mM KCl – 4.7 mM, $CaCl_2$ – 2.5 mM, $MgSO_4$ – 1.2 mM, KH_2PO_4 – 1.2 mM, $NaHCO_3$ – 25 mM, glucose – 5.5 mM). The perfusion solution was aerated with a mixture of 95% O_2 + 5% CO_2. Perfusion was conducted at 36-37°C and pH 7.3. The perfusion pressures was 75 cm water and the perfusion rate 15 ml/min. The epicardial ECG and cardiac intervalogram were recorded. After stabilization of the rhythm the heart was irrigated on its epicardial surface with Krebs–Henseleit solution, warmed to 40-41°C. The volume of irrigating solution was 10 ml. Irrigation was repeated at least 3 times, after which the ganglion blocker Arfonad (trimetaphan camsylate) was injected into the coronary circulation (10 mg in 1 ml of perfusion fluid at 36-37°C); this drug has characteristically a strong but short ganglion-blocking action. The heart was again irrigated 1-2 min after injection of Arfonad. Irrigation of the heart with a warm solution led to the development of a positive chronotropic effect, calculated by the formula: $(I_{max} - I_{orig})/I_{orig}$ (in %), where I_{orig} denotes the duration of the original P-P interval (in msec); I_{max} the duration of the shortest interval after development of the positive chronotropic effect (in msec). Altogether over 100 tests were done in 10 experiments. The data were subjected to statistical analysis by the nonparametric U test of Wilcoxon–Mann–Whitney [4].

EXPERIMENTAL RESULTS

The original heart rate in the different experiments averaged 54 beats/min (limits of variations from 4 to 94 beats/min). In the course of one experiment the variations of frequency were not significant. Irrigation of the epicardial surface with a warm solution led to an increase in heart rate, and the positive chronotropic effect averaged 20.6%. Intracoronary injection of Arfonad caused no significant changes in the original rhythm. After

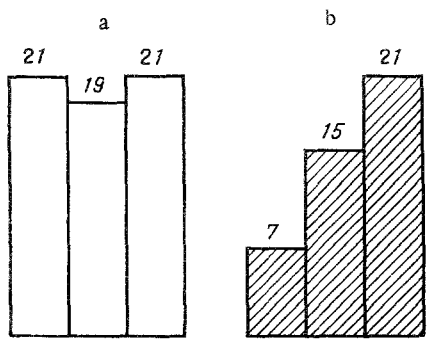

Fig. 1. Positive chronotropic effects following irrigation of the epicardial surface of the rabbit heart with warm solution before (a) and after (b) intracoronary injection of the ganglion blocker Arfonad (10 mg/ml). Unshaded column — magnitude of effects (in %) of triple irrigation of the heart before injection of Arfonad (control); shaded column — magnitude of effects (in %) of repeated irrigation of the heart 2, 4, and 6.5 min, respectively (columns from left to right) after injection of Arfonad. Results of one experiment are given.

repeated irrigations and administration of Arfonad, a significant ($p < 0.01$) reduction of the positive chronotropic effect on average by 37.9% was observed 2-3 min after injection of the ganglion blocker. This effect was followed by gradual recovery, and 5-10 min after injection of Arfonad the heart rate was virtually the same as originally (Table 1). A further injection of Arfonad caused a decrease followed by recovery of the positive chronotropic effect. Control intracoronary injection of 1 ml of perfusion fluid caused no such changes in the chronotropic effect.

Diagrams reflecting the results of one such experiment are given in Fig. 1. Initially three repetitions of irrigation with warm solution led each time to about equal quickening of the heart (the chronotropic effects were 21, 19, and 21%, respectively). The same repetition of irrigation after administration of Arfonad led to reduction of the effect 2 min after injection of the ganglion blocker to 7%, i.e., a reduction of 63% compared with the smallest original effect. The positive chronotropic effect was restored to its initial level in this experiment after 6.5 min.

The time course of changes in the chronotropic effects after injection of Arfonad in these experiments agreed well with data in the literature on the times of development of the ganglion-blocking effect and of recovery from the effect of Arfonad [7]. It can thus be tentatively suggested that the significant reduction of the positive chronotropic effects in the present experiments was connected with blocking of the intracardiac ganglia by Arfonad, and the resulting blocking of the neurogenic component of the chronotropic response of the isolated heart to a rise of temperature of the epicardial surface. Quickening of the heart rate, preserved against the background of the blocking action of Arfonad, is most probably due to a myogenic reaction of the pacemaker structures.

Under the present experimental conditions, when the epicardial surface was irrigated with warm solution, it is natural to suggest that epicardial receptors must play a leading role in the neurogenic components of the positive chronotropic response. However, the possibility cannot be ruled out that under these circumstances changes also took place in the temperature of the deeper layers — the myocardium and endocardium. Responses of different layers of the heart to changes of temperature cannot be differentiated on the basis of the data described above. However, it can be asserted on the basis of these results that afferent receptors of the heart can respond to a rise of temperature within the limits of the normal physiological variations of this parameter. Excitation of these receptors leads to activation of an intracardiac reflex, which provides for the participation of a neurogenic component in the positive chronotropic reaction of the isolated heart, deprived of its connections with the CNS.

LITERATURE CITED

1. N. N. Abushinova, G. E. Samonina, and N. M. Chernysheva, Nauch. Dokl. Vyssh. Shkoly, Biol. Nauki, No. 11, 52 (1984).
2. N. N. Abushinova, "Mechanisms of chronotropic reactions of the heart to a change in temperature of the incoming blood," Author's Abstract of Dissertation for the Degree of Candidate of Biological Sciences, Moscow (1985).
3. E. A. Gorodetskaya, G. N. Kopylova, and M. G. Udel'nov, Nauch. Dokl. Vyssh. Shkoly, Biol. Nauki, No. 11, 7 (1976).
4. E. V. Gubler and A. A. Genkin, The Use of Nonparametric Criteria in Medico-Biological Research [in Russian], Leningrad (1973).

5. G. I. Kositskii and I. A. Chernova, The Heart as a Self-Regulating System [in Russian], Moscow (1968).
6. B. S. Kulaev, The Reflexogenic Zone of the Heart and Self-Regulation of the Circulation [in Russian], Leningrad (1972).
7. M. D. Mashkovskii, Therapeutic Substances [in Russian], 7th edn. Vol. 1, Moscow (1972), p. 212.
8. Textbook of Physiology: Physiology of the Circulation: Physiology of the Heart [in Russian], Leningrad (1980), pp. 425-438.
9. M. G. Udel'nov, Physiology of the Heart [in Russian], Moscow (1975).

RELATIONSHIP OF BREATHING VARIABILITY TO VENTILATORY RESPONSE TO CARBON DIOXIDE

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KEY WORDS: breathing variability; ventilatory response to carbon dioxide; rebreathing.

Periodic fluctuations of the frequency and depth of breathing, repeated without any evident cause with a varied period, were described long ago [12]. Investigations have shown that to study the parameters of external respiration it is essential to know not only their mean values, but also the character of variations of the parameters, which is subject to the action of both physiological and stress factors [10, 11]. The nature of breathing variability has not yet been explained. It has been suggested that changes in the regularity of breathing are due to fluctuations in the activity of certain central mechanisms [6] or to manifestation of the search for energetically optimal conditions of pulmonary ventilation. Hence it is interesting to study dependence of breathing variability on the functional state of the system regulating breathing. Correlation between the partial pressure of carbon dioxide in the alveolar air (the stimulus parameter) and ventilation (the response parameter) still remains the most physiological criterion for evaluation of the function of the breathing control system in general and its sensitivity to hypercapnia in particular [1].

The aim of this investigation was to study relations between breathing variability and the ventilatory response to carbon dioxide.

EXPERIMENTAL METHOD

Tests were carried out on 35 subjects aged 25-54 years with no neurological diseases and no pathology of the respiratory and cardiovascular systems. During the investigation 13 subjects had a marked pain syndrome due to identical pathology in the hepatogastroduodenal region; nine subjects were investigated before operation, 25-45 min after receiving premedication with Moradol, whereas 13 subjects were free from complaints. To increase the accuracy of the data and to reduce the load on the subjects, the entire routine part of the investigations was automated. A program was written for the "Élektronika NTs-80" microcomputer whereby the initial signals of the pneumatochogram and capnogram could be introduced and analyzed on a realtime scale. The tests were carried out at the same time of day, when the subjects were in a state of psychoemotional rest, and seated. To prevent the subjects from drowsing, they were requested to keep their eyes open. Each investigation consisted of two parts.

1) When the breathing variability was determined, the coefficient of variation (CV = $\sigma \cdot 100\%$ M, where σ is the standard deviation and M the mathematical expectation) was chosen as the criterion to characterize this parameter, for it is independent of the absolute values of the parameters studied and can be used to compare variability of parameters differing in dimensionality.

To determine CV, after a short rest the subject was instructed to breathe through a mask connected to the transducer of a pneumotachograph. The pneumotachogram was recorded

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