EFFECT OF BLOCKING β-ADRENERGIC STRUCTURES ON THE CALORIGENIC EFFECT OF NORADRENALIN IN SKELETAL MUSCLES

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The effect of blocking β-adrenergic structures on the thermal effect of muscular contraction following intraperitoneal injection of noradrenalin in a dose of 200 μg/kg was investigated in experiments on albino rats adapted to heat (25°C) and cold (6 weeks at 2-4°C). Intraperitoneal injection of propranolol (10 mg/kg) abolishes the calorigenic action of noradrenalin on muscular contraction and both the primary and delayed heat production are reduced.

The metabolic response to cooling in an animal adapted to low environmental temperatures has been attributed to the increased calorigenic action of noradrenalin [8-11]. Noradrenalin is considered to regulate noncontractile thermogenesis, the importance of which is increased after cold adaptation, whereas the contractile activity of the muscular system no longer acts as the main source of heat. The calorigenic action of noradrenalin is mediated chiefly through β-adrenergic structures and its effect is abolished if these are blocked [5, 12, 13]. However, it was recently shown [2, 4] that noradrenalin affects the energy metabolism of muscular contraction and increases the heat production of the contractile act, to a particularly marked degree in cold-adapted animals.

The object of this investigation was to study the effect of blocking β-adrenoreceptors on the thermal effect of muscular contraction in rats after preliminary injection of noradrenalin.

EXPERIMENTAL METHOD

Noninbred male albino rats weighing 250-350 g were used. The animals of one group were kept in individual cages at a temperature of 2-4°C for 6 weeks. The animals of the other group (control) were kept during this period in a room at a temperature of 25°C.

The temperature and evoked potentials of the tibialis anterior muscle of the rats were recorded during electrical stimulation of the corresponding motor nerve. A copper-constantan thermocouple was used to record the temperature. Wire electrodes for recording the electromyogram (EMG) were placed near the working junction of the thermocouple [3].

The thermal effect of muscular contraction was estimated from the rise in temperature of the muscle during its stimulation (ΔT). Previous investigations [1] showed that the increase in temperature of a muscle in the thermoneutral zone during contraction depends chiefly on the increase in its heat production. To estimate muscular heat production it was assumed that the increase in temperature of the muscle actually during the contraction (Δt_1) takes place chiefly on account of primary heat formation, while the increase in temperature after contraction (Δt_2) takes place on account of the late phase of heat formation. Hence, $\Delta T = \Delta t_1 + \Delta t_2$. The muscle was stimulated with square pulses (3 msec, 50 Hz, 600 mV, 3 sec). Stimulation was applied at intervals of 2 min.

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The order of the experiment was as follows: the peroneal nerve was exposed under superficial ether anesthesia and the stimulating electrode applied to it. The truck of the sciatic nerve was divided above the electrode. An electrode for measuring the muscle temperature and recording the EMG was introduced into the tibialis anterior muscle. An average series of 10 stimuli was applied 30-40 min after the animal had recovered from the anesthetic and the changes in muscle temperature during each contraction were recorded. Noradrenalin was then injected intraperitoneally in a dose of 200 μg/kg body weight. The test muscle was again stimulated about 10 times from 10 to 15 min later and the changes in its temperature after each stimulation were recorded. Propranolol was then injected at once in a dose of 10 mg/kg intraperitoneally. A further 10 stimuli were then applied to the muscle after 10-15 min and its temperature was recorded. The magnitude of the stimulus remained unchanged throughout the experiment.

In the course of the experiment the animals' body temperature was monitored continously. The air temperature during the experiments was about 25°C.

Altogether 10 rats (300 muscular contractions) were used in the experiments.

EXPERIMENTAL RESULTS AND DISCUSSION

The experimental results are given in Table 1. The mean initial body temperature of the control rats was 37.0°C and of the cold-adapted rats 37.8°C.

Electrical stimulation of the motor nerve induced contraction of the tibialis anterior muscle. During contraction of the muscle its temperature rose, more so in the cold-adapted rats.

Injection of noradrenalin into the animals raised the body temperature of the control animals on the average by 1.2°C and of the cold-adapted animals by 2.8°C. The heat production of muscular contraction was increased at the same time. The temperature effect of contraction in the control group of rats averaged $32.15 \cdot 10^{-2}$°C and in the cold-adapted rats $42.97 \cdot 10^{-2}$°C. The increase in the temperature effect of muscular contraction in the animals of both groups after injection of noradrenalin took place on account of the Δt_2 component, characterizing the phase of delayed heat formation in the muscle; the increase in temperature Δt_1 during the contraction itself was not significantly changed.

Injection of propranolol into the animals caused a decrease of body temperature which averaged 0.8°C in the control rats and 1.1°C in the cold-adapted rats 20-35 min after the injection. The decrease in body temperature on the animals coincided with a decrease in the temperature effect of muscular contraction to values close to the initial level. In that case the decrease in the temperature effect of muscular contraction took place on account of both components (Δt_1 and Δt_2). After injection of noradrenalin and propranolol into the animals there was no change in the amplitude of the evoked EMG. It can accordingly be postulated that these drugs acted neither on the transmission of the stimulating impulses to the muscle nor on the magnitude of the action potentials of the muscle fibers.

The action of noradrenalin on heat production of muscular contraction and on the body temperature of the animals, which was particularly strong in the cold-adapted animals, confirms results obtained previously [2, 4]. As in investigations by other workers [5, 13], in the present experiments, blocking the β-adrenergic structures reduced the calorigenic action of noradrenalin. In previous investigations, however, the action of β-blockers was assessed purely from the body temperature and the overall gas exchange, as

TABLE 1. Effect of Noradrenalin and Propranolol on Body Temperature and Thermal Effect of Muscular Contraction in Control and Cold-Adapted Rats (M ± m)

Experimental conditions	Body temp. (°C)	Δt_1	Δt_2	ΔT
		deg · 10^{-2}		
	$n=5$	$n=50$		
Control rats:	37,0±0,4	13,14±0,64	9,65±0,98	22,79±0,85
Injection of noradrenalin	38,2±0,4	12,52±0,63	19,63±1,09	32,15±1,30
P	<0,01	>0,05	<0,01	<0,01
Injection of propranolol	37,4±0,4	9,08±0,35	14,63±0,71	23,71±0,71
P	>0,05	<0,01	<0,01	<0,01
Adapted rats:	37,8±0,3	19,42±0,79	9,91±1,14	29,33±1,55
Injection of noradrenalin	40,6±0,3	20,02±0,47	22,95±1,86	42,97±1,07
P	<0,01	>0,05	<0,01	<0,01
Injection of propranolol	39,5±0,4	14,00±0,44	14,81±1,02	28,81±1,2
P	<0,01	<0,01	<0,01	<0,01

well as from changes in the global EMG. The decrease in gas exchange after β-blocking is interpreted as a decrease in noncontractile thermogenesis and has even been proposed as a means of its quantitative evaluation [12]. The increase in the global EMG indices after injection of β-blockers is interpreted as the replacement of the blocked noncontractile thermogenesis by heat production of the contracting muscles [6, 7].

The results of the present investigation suggest that β-adrenergic structures are intermediaries in the calorigenic action of noradrenalin on muscular contraction. Blocking these structures reduces the thermal effect of muscular contraction as a whole. That is why the decrease in heat formation in the whole organism under the influence of β-adrenergic blockers cannot be used to assess noncontractile thermogenesis. The increase in contractile activity of the muscles after blocking of the β-structures can be explained by the need to compensate the reduced heat production of the elementary muscular contraction brought about by the action of the β-blockers.

Whereas the decrease in secondary heat formation under the influence of propranolol can readily be explained by blocking of the calorigenic action of noradrenalin, the mechanism of the action of propranolol on primary heat formation still remains unexplained. In addition, the results of these experiments do not rule out the participation of β-adrenergic structures in possible changes in heat production in other organs, a subject which requires special investigation.

LITERATURE CITED

1. K. P. Ivanov, E. Ya Tkachenko, and M. A. Yakimenko, Fiziol. Zh. SSSR, 56, 1438 (1970).
2. E. Ya. Tkachenko and M. A. Yakimenko, Fiziol. Zh. SSSR, 57, 1540 (1971).
3. M. A. Yakimenko, Fiziol. Zh. SSSR, 56, 1861 (1970).
4. M. A. Yakimenko, E. Ya. Tkachenko, K. P. Ivanov, et al., Dokl. Akad. Nauk SSSR, 200, 1007 (1971).
5. R. Bertin and J. Le Blank, J. Physiol. (Paris), 60, 349 (1968).
6. K. Brück and B. Wünnenberg, Pflug. Arch. ges. Physiol., 282, 376 (1965).
7. K. Brück and Wümenberg, Fed. Proc., 25, 1332 (1966).
8. W. N. Cottle and L. D. Carlson, Proc. Exp. Biol. (New York), 92, 845 (1956).
9. J. S. Hart, in: Proceedings of the Twenty-Second International Congress at Physiological Sciences, Vol. 1, Amsterdam (1963), p. 398.
10. A. C. L. Hsieh, L. D. Carlson, and G. Gray, Am. J. Physiol., 190, 247 (1957).
11. L. Jansky, R. Bartunkova, and E. Zeisberger, Physiol. Bohemoslov., 16, 366 (1967).
12. J. Mejsnar and L. Jansky, in: Nonshivering Thermogenesis (International Symposium), Prague (1971), p. 27.
13. R. Porter, R. Berlin, M. C. Laury, et al., in: Nonshivering Thermogenesis (International Symposium), Prague (1971), p. 57.