PHYSIOLOGY

Effects of Urethane Anesthesia on the Thresholds of Thermoregulatory Reactions

E. Ya. Tkachenko and T. V. Kozyreva

Translated from *Byulleten' Eksperimental'noi Biologii i Meditsiny,* Vol. 127, No. 3, pp. 248-251, March, 1999
Original article submitted May 28, 1998

Rats without anesthesia and those superficially anesthetized with urethane responded to rapid cooling by two-phase metabolic reactions without changes in core temperature and heat emission. Their vascular reactions started much later than metabolic reactions. In animals under deep urethane anesthesia, vascular response occurred prior to metabolic response without changes in core temperature. Metabolic reaction became monophasic and occurred much later, with the lowering of rectal temperature. An increase in oxygen consumption coincided with an increase in muscle contractile activity. It is concluded that deep urethane anesthesia not only delays metabolic reactions but also changes the sequence of thermoregulatory reactions.

Key Words: *urethane anesthesia; thermoregulation; cooling; reaction thresholds*

The interest in the effects of anesthesia on thermoregulatory reactions is stimulated by the necessity of producing analgesia and immobilization in animal experiments and surgical interventions in humans, including those performed under hypothermic conditions.

General anesthetics are known to suppress the activity of the central brain structures and behavioral reactions responsible for the body temperature control. They slow down metabolic processes and lower body temperature even under thermoneutral conditions [6]. However, the interrelations between the depth of anesthesia and the structure and thresholds of thermoregulatory reactions to cooling have not been studied in detail.

In this work we compared the thresholds of cold-defence reactions in non-anesthetized (control) and urethane-anesthetized rats exposed to rapid cooling, which is usually accompanied by a dynamic response of skin cold receptors.

Institute of Physiology, Siberian Division of the Russian Academy of Medical Sciences, Novosibirsk

MATERIALS AND METHODS

Experiments were carried out on male albino rats weighing 200-250 g. In control rats (group 1, n=31), all preliminary manipulations, such as implantation of recording probes and fixation on a thermocontrolled table were performed under Rausch ether narcosis. The experiments were started after complete recovery from narcosis. Group 2 rats (n=27) were given intraperitoneal injections of urethane (1 g/kg), after which oxygen consumption under thermoneutral conditions decreased by 15%. Group 3 rats (n=25) were subjected to deeper urethane anesthesia by giving them an initial dose (1.3 g/kg) with repeated injections of one-half of this dose every 1-1.5 h. This schedule produced a 25% reduction of metabolism.

During the experiment rat was placed on a thermocontrolled table, and abdominal skin temperature was maintained at 37±0.12°C. Basal indices were recorded for 10 min (Table 1). Then the abdominal skin area of 25 cm^2 was cooled to 24°C at a rate of 0.03-0.05°C/sec using a water thermode and maintained at this level for 15-20 min.

0007-4888/99/0003-0223$22.00

TABLE 1. Basal Indices of Nonanesthetized and Anesthetized Rats at Neutral Temperature (*M±m*)

Parameter	Control	Anesthesia	
		superficial	deep
Oxygen consumption, ml/min/kg	23.8±1.88	20.7±0.70	18.4±0.67
Temperature, °C			
rectal	36.9±0.24	36.6±0.15	36.5±0.10
intradermal in the cooling area	35.2±0.22	36.6±0.31	37.0±0.12
skin	34.5±1.1	33.8±0.4	30.5±0.5

The following indices were continuously monitored during cooling: skin temperature in a distant region (it allowed us to determine the start and intensity of vascular reactions to cooling directed toward reduction of heat emission), rectal temperature, intradermal temperature in the area exposed to cooling, and total oxygen consumption. Additionally, electrical activity of neck muscles was recorded in experiments with deep anesthesia, which allowed us to identify the mechanism of cooling-induced increase in heat production. The parameters were recorded as described previously [2,3]. The thresholds for vascular, metabolic and muscular reactions were determined by changes in the basal indices by 0.1°C, 1 ml/min/kg and 1 μV, respectively. All the indices were recorded by a computer with laboratory-developed software.

The study included 83 experiments on 58 animals. The data were analyzed statistically using Student's *t* test.

RESULTS

In the rats of groups 1 and 2, cooling by 4.5-5°C induced a rapid metabolic reaction without changes in core temperature and heat emission (Table 2, Fig. 1).

Oxygen consumption increased in two phases. During the first phase it rose at a rate of 7.2±1.9 ml/min/kg with the maximum increment of 8.3 ml/min/kg (41% of the initial value). The second phase started with a 0.46±0.11°C decrease in rectal temperature, the maximum increment being 14.4±1.4 ml/min/kg (70%). Thus, cooling induced more than a 110% increase in oxygen consumption.

Vascular reactions occurred much later than metabolic response, when rectal temperature decreased by 0.3-0.5°C. The latencies of vascular reactions in groups 1 and 2 were similar. The threshold was skin cooling by more than 8°C (Table 3).

In group 3 with deep anesthesia, the metabolic reaction occurred considerably later than in groups 1 and 2 with intradermal temperature lowering by 11.5°C. In this period rectal temperature was also lowered. The metabolic curve became monophasic. The maximum increment of oxygen consumption was 71%. The increase in heat production was accompanied by intensification of muscular contractions (Table 2, Fig. 1).

In rats under deep anesthesia, vascular reactions to cooling preceded the metabolic response and occurred at higher intradermal temperature of the cold-exposed area, than in control and superficially anesthetized rats (Table 3, Fig. 1); the core temperature was unaffected.

In our experiments, the superficial urethane anesthesia, which reduced metabolic processes by 15%, left thermoregulatory thresholds unaffected. Deep anesthesia delayed metabolic reactions, thus changing the structure of the thermoregulatory responses.

The metabolic reaction was predominant under superficial urethane anesthesia. It occurred as a first response to cooling, reached a high level and had a

TABLE 2. Parameters of Metabolic Reaction during Cooling (*M±m*)

Parameter	Control	Anesthesia	
		superficial	deep
Latency, sec	42.1±6.9	40.8±4.8	637±71.3**
Threshold decrease in temperature, °C			
intradermal, in the cooling area	5.1±0.59	4.0±0.36	11.5±0.76**
rectal	0.017±0.009	0.025±0.016	2.1±0.25
Maximal oxygen consumption increment, ml/min/kg	26.2±1.8	22.7±1.7+	13.1±0.91**

Note. Here and in Table 3: +$p< 0.05$ in comparison with the control; *$p<0.05$, **$p<0.01$ in comparison with superficial anesthesia.

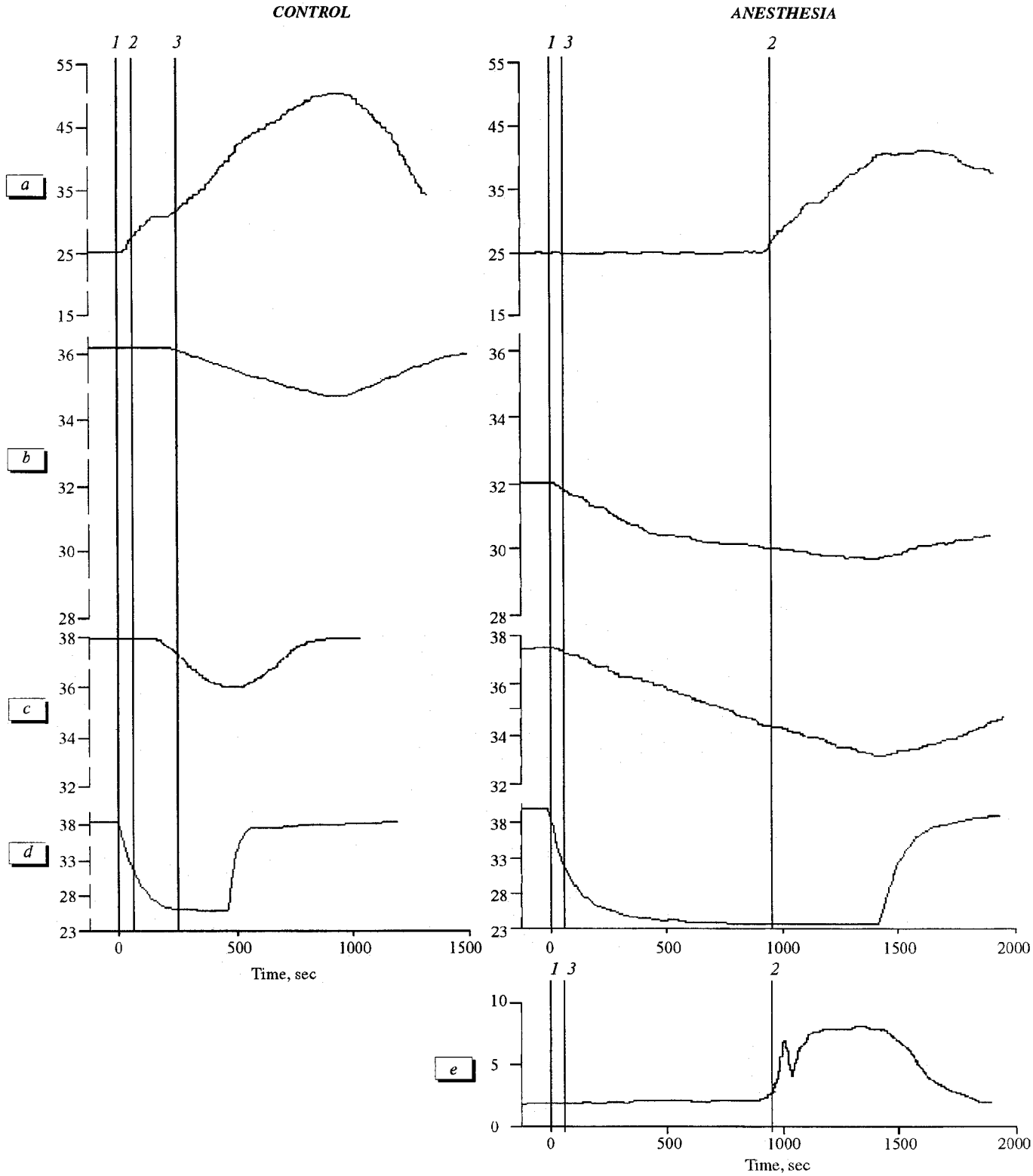

Fig. 1. Development of metabolic and vascular reactions to cooling in control and anesthetized rats. *a)* oxygen consumption; *b)* ear skin temperature; *c)* rectal temperature; *d)* intradermal temperature in the cooling area; *e)* electrical activity in the neck muscles. *1)* start of cooling; *2)* start of metabolic reaction (an increase in the total oxygen consumption and muscular activity); *3)* start of vascular response (ear skin vasoconstriction and temperature decrease).

TABLE 3. Parameters of Vascular Reaction during Cooling (*M±m*)

Parameter	Control	Anesthesia	
		superficial	deep
Latency, sec	207.7±37.6	256±38.0	70.0±4.4**
Threshold decrease in temperature, °C			
intradermal, in the cooling area	8.6±0.13	8.1±0.15	5.6±0.21**
rectal	0.31±0.08	0.54±0.15	0*
Maximal skin temperature decrement, °C	1.1±0.11	1.2±0.13	1.7±0.08*

two-phase time course. It was shown that the two-phase metabolic reaction is associated with the dynamic activity of skin cold receptors [1]. The first phase of heat production, which is suggested to arise from nonshivering thermogenesis [4,5], disappeared in the absence of dynamic response of cold receptors, for instance under conditions of slow cooling [2]. The absence of the first phase under deep anesthesia may be due to suppression of nonshivering thermogenesis. This suggestion is supported by the observation that under deep anesthesia the increase in heat production coincides with the increase in muscle contractile activity. It cannot be excluded that deep anesthesia suppresses the effector response to the dynamic signal of skin thermoreceptors. Stronger simulation of central thermosensitive elements is probably needed for the development of the metabolic response under these conditions, which can be achieved by considerable lowering of core temperature.

The dynamic component seems to play different role in the development of vascular responses to rapid cooling. As shown previously [2], the threshold temperature for vascular reactions is inversely proportional to the rate of cooling, i.e., dynamic activity of skin cold receptors suppressed the vascular response. In nonanesthetized animals, vascular response coincided with the beginning of the second phase of metabolic response, while under deep anesthesia it occurred much earlier, as if to compensate for the absence of metabolic reaction at unchanged core temperature. It should be noted that our results do not agree with published data showing an anesthesia-induced decrease in the temperature thresholds for both cold-defence reactions [7]. This discrepancy can be attributed to specific effects of urethane anesthesia on vascular responses.

Thus, deep urethane anesthesia not only delays metabolic reactions but also changes the sequence of thermoregulatory responses.

REFERENCES

1. T. V. Kozyreva and L. A. Verkhoglyad, *Fiziol. Zh. SSSR*, **75**, No. 1, 117-123 (1989).
2. T. V. Kozyreva and L. A. Verkhoglyad, *Ros. Fiziol. Zh.*, **83**, No. 11-12, 135-142 (1997).
3. P. V. Lazarenko and V. E. Divert, in: *The New Methods of Medical Practice and Biomedical Research* [in Russian], Novosibirsk, 25-28 (1983).
4. L. Jansky, *Biol. Rev.*, **75**, No. 2, 237-259 (1995).
5. I. B. Mekjavic, A. La Prairie, A. Burke, and B. Lindburg, *Respir. Physiol.*, **70**, No. 1, 121-130 (1987).
6. C. F. Roe, in: *Physiological and Behavioral Temperature Regulation*, Eds. J. D. Hardy *et al.*, New York, 727-740 (1970).
7. D. I. Sester, in: *Thermal Balance in Health and Disease*, Eds. E. Zeisberger *et al.*, Basel, Boston, Berlin, 251-263 (1994).