MECHANISMS OF ONSET OF MORPHOLOGICAL CHANGES IN THE CNS IN UNANESTHETIZED ALBINO RATS COOLED BY VARIOUS METHODS

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Changes in temperature regulation were compared with morphological changes in various parts of the CNS of unanesthetized albino rats cooled by different methods. The role of afferent impulses from the cooled tissues and of thermoregulatory excitation of nervous structures in the genesis of morphological changes in neurons of the reticular formation, mammillary bodies, and spinal cord was established. Morphological changes in cortical neurons are evidently due to the direct action of cold on the brain.

KEY WORDS: hypothermia; neurons of the CNS; temperature regulation.

Data on morphological changes in the CNS of unanesthetized animals during hypothermia are limited [1, 2]. There is no information on brain pathomorphology associated with different methods of cooling. Little likewise is known of the mechanisms of the morphological disorders at different levels of the CNS.

The object of this investigation was to compare thermoregulatory changes in the body with morphological changes in various parts of the CNS in unanesthetized albino rats cooled by different methods.

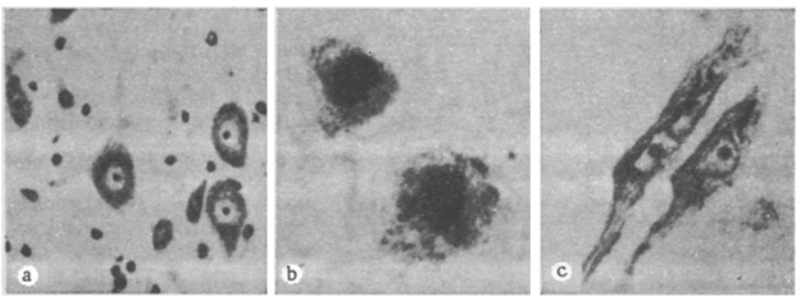

Fig. 1. Neurons of mesencephalic reticular formation of unanesthetized albino rats (stained by Nissl's method): a) control rat, 230 ×; b) general cooling to 30°C: hyperchromia of nucleus, pulverization and lysis of tigroid, 600 ×; c) cooling of body combined with warming of head: shrinking of neurons; fragmentation and partial liquefaction of tigroid; deformation of nuclei; staining and swelling of processes, 900 ×.

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TABLE 1. Thermoregulatory Changes in Body and Morphological Changes in CNS of Unanesthetized Albino Rats Cooled by Different Methods (M ± m)

Method of cooling	Thermoregulatory changes		Temperature (deg)				Morphological changes in different parts of CNS*				
	oxygen demand (ml/kg · min)	electrical activity of muscles (conventional units)	rectal	skin	in CC	in RF (at end of cooling)	CC	AH	PH	RF	SC
Initial state	42,7±2,1 (100%)	8,19±0,21 (100%)	37,7±0,3	36,4±0,4	37,4±0,2	37,6±0,3	—	—	—	—	—
General cooling	63,5±2,3 (149%)	20,85±0,67 (254%)	30,0±0,0	28,2±0,2	31,9±0,2	33,0±0,2	23±3 8±1	31±2 17±2	72±4 21±2	92±5 66±3	48±2 23±3
Cooling of head	52,5±1,9 (123%)	16,78±0,42 (205%)	30,0±0,0	34,2±0,1	19,6±0,0	21,4±0,1	46±5 37±4	43±4 29±2	38±3 9±1	50±4 31±3	28±2 14±2
Cooling of head with warming of body	46,5±2,1 (109%)	11,13±0,31 (136%)	35,9±0,4	37,3±0,3	21,4±0,1	22,6±0,1	45±3 34±3	68±4 36±3	44±4 18±2	32±3 24±3	8±0 3±0
Cooling of body with warming of head	59,7±1,8 (140%)	20,88±0,34 (255%)	30,0±0,0	28,6±0,3	36,0±0,2	35,8±0,3	20±2 10±1	26±2 19±2	70±5 24±3	96±6 71±5	47±3 25±2

*Numerator VL, denominator SL.

EXPERIMENTAL METHOD

Unanesthetized albino rats (180-250 g) fixed in wire cages were exposed to cooling of the whole body (24 rats), isolated cooling of the head (16), cooling of the head with warming of the trunk (12), or cooling of the whole body and warming of the head (11). The trunk or head of the rats (corresponding to the method of cooling) was covered with polyethylene bags containing a mixture of ice and salt (4-7°C) or with hot water bottles (38-40°C). With all methods of cooling (except cooling the head and warming the trunk) the rectal temperature fell to 30°C. The duration of cooling was 120 ± 3 min. The skin temperature (in the region of the outer third of the thigh) and brain temperature (in the cortex and in the mesencephalic reticular formation; in the latter case corresponding to stereotaxic coordinates AP = 5, H = 7.5, L = 1.5 [8]) were measured before and after cooling by means of electrical resistance thermometers. The oxygen demand was determined in a closed chamber [7]. Electrical activity of the muscles (EAM) also was recorded as the frequency of muscular oscillations and their area in integrator units [3].

After cooling, the animals were killed for histological examination of neurons (celloidin sections stained by Nissl's method, preliminary fixation in Carnoy's fluid) of the cerebral cortex (CC), the preoptic region of the anterior hypothalamus (AH), the mammillary bodies of the posterior hypothalamus (PH), the mesencephalic reticular formation (RF), and the cervical portion of the spinal cord (SC). In frontal brain sections the number of slightly and considerably changed neurons was counted in every hundred neurons. The following parameters were used: the volume of the lesion (VL) – the total number of altered neurons per 100 in a particular part of the brain, and the severity of the lesion (SL) – the number of severely changed neurons in 100 examined.

EXPERIMENTAL RESULTS AND DISCUSSION

During whole-body cooling, as well as during cooling of the body combined with warming of the head, considerable morphological changes (chromatolysis to a varied degree, hypochromia and hyperchromia of the neurons or their parts, increased basophilic staining of the nucleus, an eccentric position of the nuclei and nucleoli, etc.) were observed in the neurons of RF, PH, and SC (Fig. 1). In the CC and AH neurons the morphological changes were relatively slight.

After isolated cooling of the head or cooling of the head combined with heating of the trunk, considerable morphological changes occurred in the CC and AH neurons, whereas morphological changes in the RF, PH, and SC neurons were relatively slight (Table 1).

The most severe morphological changes in CC and AH neurons occurred in the experiments in which the brain temperature fell considerably, and changes in RF,

PH, and SC neurons occurred after cooling of the body, i.e., when methods of cooling were used in which an increased flow of afferent impulses could have reached the nervous centers [5, 6, 9] and induced their thermoregulatory excitation [4]. This is shown by an increase in the intensity of the thermoregulatory responses, manifested as an increase in the oxygen demand and the electrical activity of the nuscles. After general cooling of the animals the brain temperature also fell, but this factor evidently did not play an essential role, for when the head was warmed and the brain temperature was maintained at a relatively high level, the severity of the morphological changes in the RF, PH, and SC neurons was the same as after cooling of the whole body. The temperature gradient between the cerebral cortex and brain stem was only 1.1° after cooling of the whole body, but 1.8° after isolated cooling of the head. The temperature differences between the superficial and deeper parts of the brain thus could not have played an essential role in the production of the morphological changes.

The facts described above indicate the importance of the brain stem and spinal cord in the regulation of heat metabolism during exposure to low temperatures. Neurons of the cerebral cortex evidently are the most sensitive to the direct action of cold on the CNS.

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