Cardiovascular and Respiratory Responses to Cooling of the Medulla Oblongata of the Cat[1] (34878)

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In a previous study (1), one of us demonstrated that warming certain neural elements in the lateral reticular formation of the medulla oblongata of the cat produced tachycardia, slight hypertension, and respiratory inhibition. The present investigation is an attempt to determine whether these neural elements also respond to cooling.

Materials and Methods. Twenty cats were anesthetized by intraperitoneal injection of urethane (0.8–1.0 g/kg). Rectal temperature was maintained at about 38° by an electric heater controlled automatically by a Klixon 5CT3 proportional thermoregulator. The trachea was cannulated and both vague nerves were dissected free of surrounding tissue. The right femoral artery was cannulated and the arterial pressure was monitored with a Statham P23AC transducer. Heart rate was monitored with a Grass 5P4 tachograph unit which was triggered by the arterial pulses. Respiratory movements were monitored with a chest pneumograph, connected to a Statham P23BC transducer. All recordings were made on a Grass 5B polygraph.

The head of the cat was placed in a stereotaxic instrument. The medulla oblongata was cooled as follows:

1. For general cooling the dorsal and ventral surfaces of the medulla were irrigated with cold physiological saline (25–20°). For irrigation of the dorsal surface of the medulla, the cat was placed in a prone position, a portion of the occipital bone was removed, and caudal part of the cerebellum was retracted to expose the dorsal surface of the medulla. For irrigation of the ventral surface of the medulla, the cat was placed in a supine position, the muscles around the pharynx and larynx were dissected free, and part of the basilar portion of the occipital bone and the underlying dura were removed to expose the ventral surface of the medulla. A copper-constantan thermocouple, mounted in a 20-G tubing (1), was positioned 1 mm below the brain surface to monitor changes in brain temperature during irrigation.

2. Local areas were cooled by removing the heat load of the brain tissue by conduction. In a few preliminary experiments a 19-G metal tubing attached to a Borg-Warner cryosurgical unit was inserted to the desired area of the medulla for cooling. It was found later that the same cooling could be more effectively achieved by direct application of dry ice over the upper part of the 20-G tubing mounted with the thermocouple inside. Thus, the effective temperature at the tip of the tubing was monitored. Since the tubing was insulated except at the tip, it could be used as a unipolar electrode for electrical stimulation as well.

To compare the effects of general or local cooling of the medulla with the effects of warming, the surfaces of the medulla were irrigated with warm physiological saline, or local regions were heated by diathermy.

At the end of the experiment the cat was killed and the head was perfused with 10% formalin. The area of the brain that was

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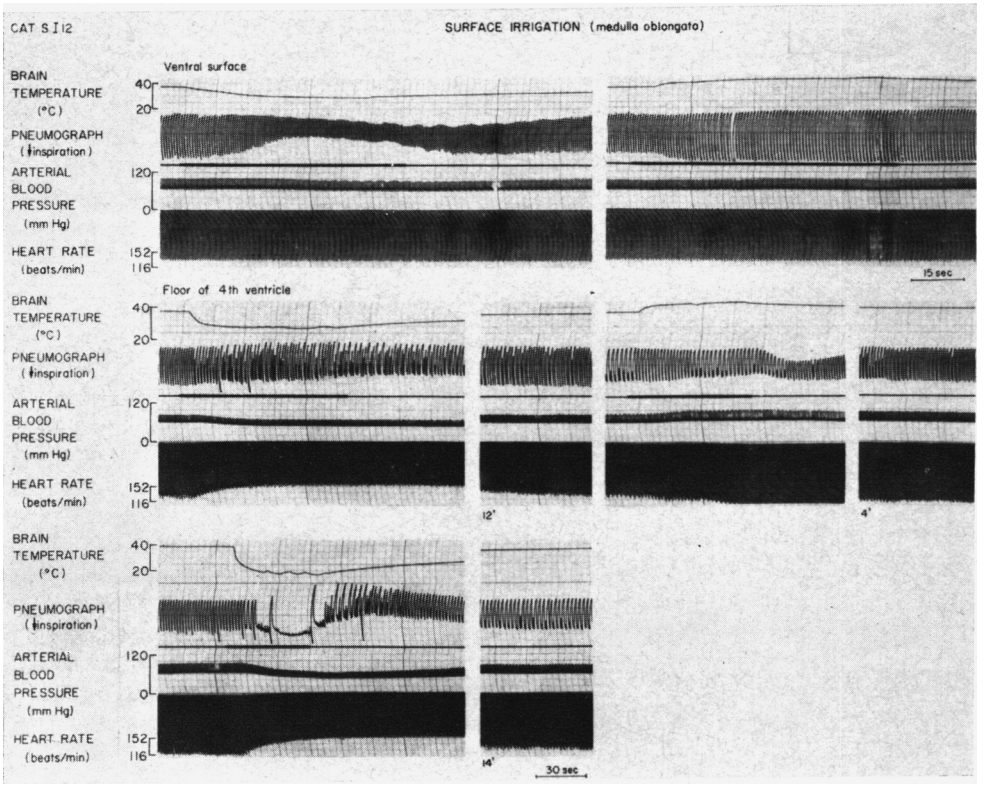

FIG. 1. Effects of irrigation on the ventral and dorsal surface of the medulla oblongata. Upper panel: Irrigation of the ventral surface with cold (left half) and warm (right half) saline. Note the respiratory responses and practically no cardiovascular reactions. Middle and lower panels: Irrigation of the dorsal surface with cold (left half) and warm (right half) saline. Note the hypotension, cardioacceleration, and respiratory acceleration during cold irrigation and hypertension and bradycardia during warm irrigation.

thermally activated was frozen. Serial sections of 50-μ thickness were cut and stained by the Weil method.

Results. Surface irrigation. Figures 1, 3, and 4 show the effects of irrigation of the floor of the fourth ventricle with cold saline. When the temperature on the dorsal surface of the medulla was lowered to about 25°, the most conspicuous effects were tachycardia and mild hypotension. The respiratory amplitude was decreased but the rate was increased (Fig. 1, upper panels). When the temperature was lowered further to about 20°, the depressor responses became more prominent but the respiration ceased with occasional gasping (Fig. 1, lower panels). In the same animal, irrigating the dorsal surface with warm saline to about 43° produced bradycardia, slight hypertension and inhibition of respiration. When the ventral surface of the medulla was irrigated with either cold or warm saline, similar changes in respiration occurred but the cardiovascular reactions were not clearly evident.

Local cooling. When the lateral reticular formation was cooled locally, the same cardiovascular responses were observed as with surface irrigation of the dorsal medulla. Local heating of the same area with high-frequency current produced bradycardia, hypertension, and apnea (Fig. 2, upper panels). Electric stimulation of this area produced no cardiovascular reactions. On the other hand, when the cooling tube was raised and the paraventricular gray matter was cooled or warmed, there was no observed cardiovascular changes. Electrical stimulation, however, produced bradycardia (Fig. 2, lower panel).

Nature of the cooling response. In five cats, cardiovascular and respiratory responses

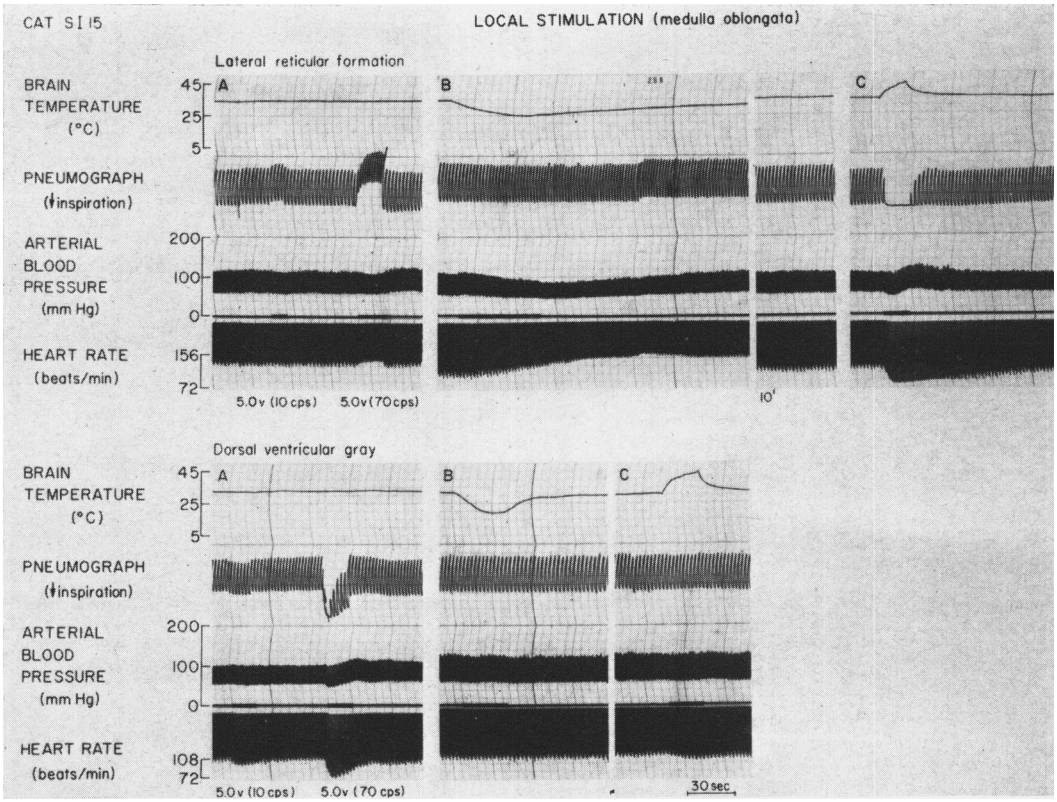

FIG. 2. Effects of local cooling and heating of the medulla oblongata. Upper panels. The electrode was placed in the lateral reticular formation. A. Stimulation with 5 V and rectangular wave pulses of 10 and 70 cps. Note the absence of cardiovascular responses. B. Cooling (25°) of the same area. Note the hypotension and cardioacceleration. C. Diathermy (44°) of the same area. Note the hypertension, bradycardia, and respiratory inhibition. Lower panels. The electrode was placed in the dorsal ventricular gray matter. A. Stimulation with 5 V and 10 and 70 cps. Note the bradycardia. B and C. Cooling (24°) and (44°) of the same area. Cardiovascular changes were insignificant.

to cooling and warming the lateral reticular formation of the medulla were compared before and after midcollicular decerebration. This procedure did not alter the cardiovascular and respiratory responses to both cooling and warming (Fig. 3, left lower panels). Artificial ventilation also did not alter the responses (Fig. 3, middle lower panels). Vagotomy eliminated the tachycardia caused by cooling (Fig. 4, lower panels). The latter procedure, however, had little effect on the hypotensive reaction.

Discussion. Numerous studies have been made on the physiological responses of the brain to temperature changes, particularly to a rise in temperature (2, 3). The temperature of the brain has been raised by warming the blood in the common carotid (4, 5) or vertebral arteries (6), or by irrigating the brain surface with warm saline (7). Magoun *et al.* (8) utilized diathermy to warm a small circumscribed area in the preoptic region and hypothalamus to produce polypneic panting. They noted that the reactive elements appeared to be concentrated in the preoptic region, and mild responses also appeared in its caudal extension in the posterior hypothalamus and the rostral portion of the midbrain. Hemingway *et al.* (9) confirmed the observation of Magoun *et al.* (8) in unanesthetized animals. Freeman and Davis (10) and Hammel *et al.* (11) have extended their studies to cooling of the hypothalamus.

In addition, Nakayama *et al.* (12) demonstrated that in the anterior hypothalamus the firing rate of thermal-sensitive neurons in-

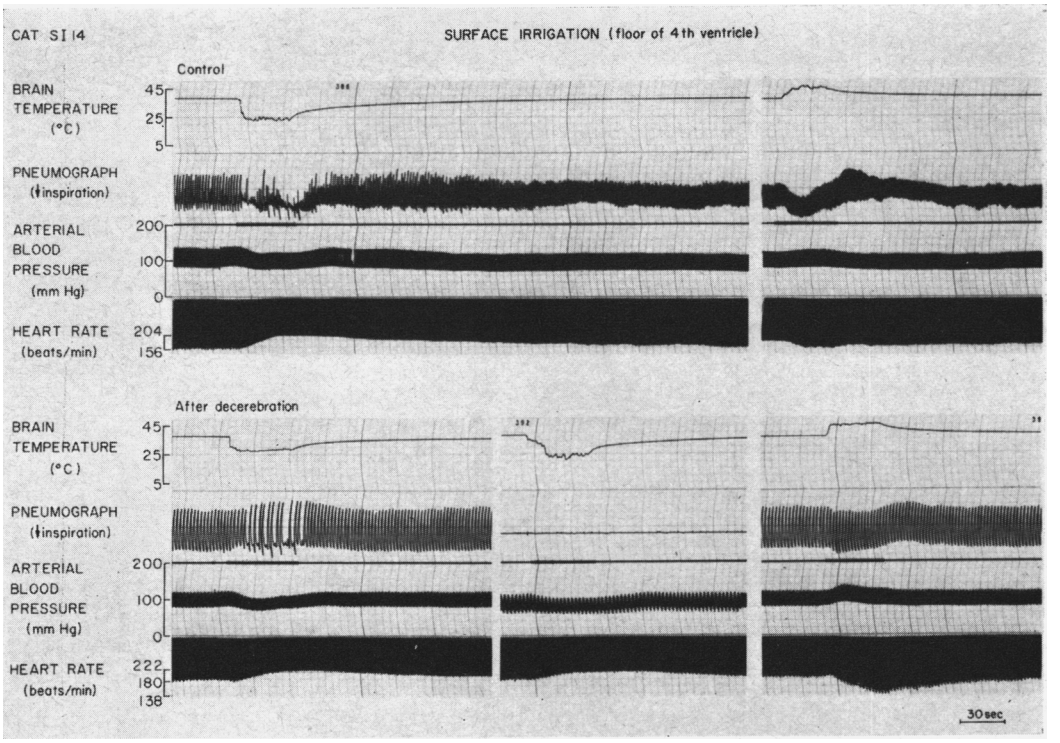

FIG. 3. Effects of midcollicular decerebration on surface irrigation of the floor of fourth ventricle. Upper panel. Control responses of irrigation with cold (left) and warm (right) saline. Lower panel. Cooling (left) and warming (right) responses after decerebration. Note the same changes after the decerebration. Middle trace shows the same cardiovascular responses when the animal was artifically ventilated.

creased proportionally with the increase in brain temperature. In the same area, Wit and Wang (13) found that some neurons showed a progressive reduction in unit activity when brain temperature was increased. They also found neurons whose firing rate increased with increased cutaneous temperature.

However, there are other thermally sensitive neural structures besides those in the preoptic area and the hypothalamus. Holmes *et al.* (14) reported a depressor response in cats when the medial reticular formation was heated by diathermy. In a previous study (1), it was reported that when the lateral reticular formation of the medulla oblongata was heated, the most marked responses were bradycardia and respiratory inhibition. When the same area was electrically stimulated, however, only a forced inspiratory response without any obvious cardiovascular changes was observed. In the present study, we have again demonstrated the presence of thermosensitive elements in the medulla oblongata which are responsive to cooling. It appears that the same neural structures respond to both heat and cold. Cooling of the lateral reticular formation of the medulla produced effects (tachycardia, mild hypotension, and respiratory acceleration) opposite to those of warming.

In agreement with our previous findings, these effects of cooling do not involve the thermoregulatory mechanisms of the rostral brain structures as these responses are observed in the decerebrate preparations. The tachycardia results from altered vagal activity since it is eliminated by vagotomy. On the other hand, the hypotensive reaction is most likely effected through inhibition of sympathetic activity. Furthermore, the cardiovascular and respiratory responses are independent of each other. The results indicate that cer-

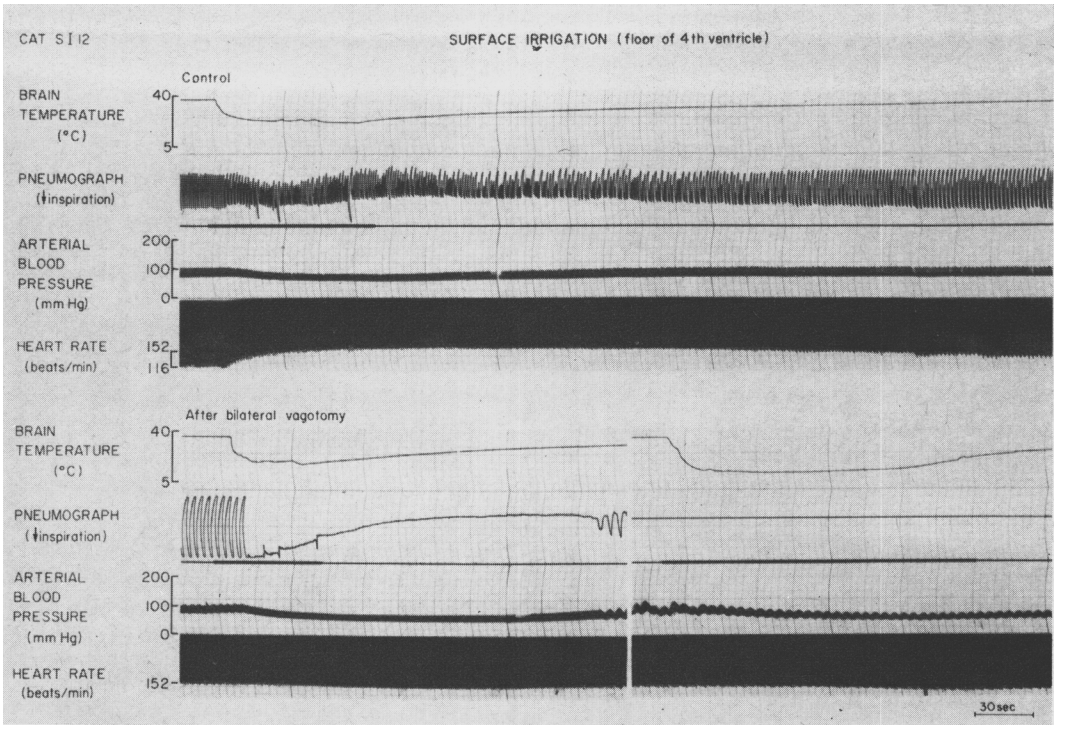

FIG. 4. Effects of vagotomy on cooling the medulla oblongata. Upper panel. Control cooling responses. Lower panel. Cooling responses after bilateral vagotomy (left). Note persistence of hypotension, but absence of cardioacceleration. The hypotension was also unaffected when the animal was artificially ventilated (right).

tain neurological elements in the lateral reticular formation of the medulla oblongata are affected by changes in brain temperature.

At present, it is difficult to assess the functional significance of the responses to cooling and warming of the medulla. Since they are produced by markedly lowering the brain temperature, it seems reasonable to assume that thermosensitive mechanisms in the medulla oblongata are important only during extreme temperature changes.

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