

Vasomotor Responses from Application of Drugs to the Medullary Region.

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Since Cushing¹ reported that injections of pituitrin and of pilocarpine into the human brain ventricles gave similar effects, numerous workers have concerned themselves with the idea that these drugs may give a central action quite different from that following peripheral administration. Many investigators have injected various drugs into almost all parts of the central nervous system, the results, however, were by no means consistent.

Heller^{2, 3} reported a negative or small depressor response in cats under urethane anesthesia when 1.5 mg of adrenaline was injected intracisternally, while in dogs a small pressor reaction was obtained with 4 pressor units of pitressin. Histamine (one mg) and acetylcholine (10 r) were reported to be centrally inactive. Haraguchi,⁴ on the other hand, found that 1% of acetylcholine or pilocarpine directly applied to the surface of medulla of cats produced a definite depressor response and augmented respiration. The central effect of acetylcholine (0.1-1 r) in cats under paraldehyde or urethane anesthesia was claimed by Dikshit⁵ to be inconsistent. According to the recent work of Suh and others⁶ on dogs under chloralose anesthesia, 4-40 r acetylcholine given intracisternally or applied on the floor of the fourth ventricle gave an elevation of blood pressure and an augmentation of respiration. The present communication deals with the central action of a group of sympathomimetic and parasympathomimetic drugs on blood pressure and respiration of cats. The cisternal region and the floor of the fourth ventricle were chosen as the sites of administration.

In this series of 17 cats, nembutal (20 mg per kilo) was given to produce a light anesthesia. The cisternum was exposed by removing part of the occipital bone. Usually several applications of drugs were made to the cisternal region before the cerebellum was finally retracted or extirpated to expose the floor of the fourth ventricle.

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¹ Cushing, H., *Proc. Nat. Acad. Sci.*, 1931, **17**, 163.

² Heller, H., *Arch. Exp. Path. Pharmacol.*, 1933, **173**, 291.

³ Heller, H., und Kusunoki, G., *Ibid.*, 1933, **173**, 301.

⁴ Haraguchi, S., *Nagasaki Igakkwai Zassi*, 1933, **11**, 191.

⁵ Dikshit, B. B., *J. Physiol.*, 1934, **80**, 409.

⁶ Suh, T. H., Wang, C. H., and Lim, R. K. S., *Chin. J. Physiol.*, 1936, **10**, 61.

TABLE I.
Varieties of Responses to Different Drugs.

Drug	Amt.		Site	No. of cats			Avg B.P. change in mm Hg among depressor responses
	cc	Pressor units		Total	Negative	Pressor	
Pituitrin	.2	2	IC*	15	2	4	-15
			IVth†	6	1	1	-13
Pitressin	.2	4	IC	4	1	1	-18
			IVth	6	1	1	-11
Pitocin	.2	0	IC	4	2	1	-15
			IVth	5	2	1	-12
Pilocarpine	.2	.2 mg	IC	4	4	0	0
			IVth	9	6	0	-11
Histamine	.2	.2 mg	IC	5	0	1	-35
			IVth	7	3	0	-21
Acetylcholine	.2	20-100 r	IC	10	3	2	-15
			IVth	14	4	3	-18
Adrenaline	.2	.2 mg	IC	5	2	1	-10
			IVth	9	3	4	-15
Physiological saline solution	.2	0	IVth	4	4	0	0

*IC—intracisternal application.

†IVth—application to the floor of the fourth ventricle.

The drugs were delivered over its surface with a tuberculin syringe and needle. Mechanical stimulus was carefully avoided, and no 2 applications were made within a single 30-minute interval. Physiological saline solution was occasionally applied as a control. The right carotid artery was cannulated and connected with a mercury manometer for blood pressure and a tracheal cannula connected to a tambour was inserted to record respiratory movements.

From the data, one can see that there is no characteristic difference in response obtained by administration of drugs through these two routes. Among 31 trials with pituitrin and pitressin, an immediate depressor response (11-18 mm Hg) was observed in 19 cases, but when these drugs were injected intravenously, a definite pressor response was obtained. Responses to pitocin and adrenaline were variable, and pilocarpine was rather inactive. All the pressor reactions so far obtained were small and delayed with a period of latency of at least 30 seconds. Since the drugs themselves have a peripheral sympathomimetic action, it is possible that they were slowly absorbed into the blood stream and acted peripherally. Histamine gave a marked depression of blood pressure (21-35 mm Hg) in 8 of the 12 cases. It is of interest that the other parasympathomimetic drug, acetylcholine, also produced a depressor response of 15-18 mm Hg in a large number of cases, but 5 out of 24 trials showed a simple delayed pressor reaction. We were unable to observe a definite vasomotor change with acetylcholine of less than 20 r. The respiration as far as the rate and excursion were concerned showed no conspicuous change throughout this series.

We have no satisfactory explanation for the great divergence of results among our own and other workers. It seems to us that other than the difference in the species of the animal used and the dosage of drugs, the degree and type of anesthesia are of great importance in determining the variability of response.⁷ It is possible that the drugs act non-specifically and that pressor or depressor responses are dependent upon the degree of selective depression of the vasomotor centers (pressor or depressor) as a result of the anesthesia.

Summary. Small doses of pituitrin, pitressin, histamine and acetylcholine when applied to the cisternal space or the floor of the fourth ventricle of cats under light nembutal anesthesia usually give a small depressor response. The effects of pitocin and adrenaline are inconsistent. Pilocarpine is inactive. There is occasionally an unexplained delayed pressor response with central application of acetylcholine.

⁷ Jackson, D. E., *J. Lab. Clin. Med.*, 1934, **20**, 1.