The Effect of Vasopressine on the Circulation of the Rat Organs, with Special Consideration of the Skin

According to a widespread opinion, vasopressine has no part in the regulation of the circulation, in view of the fact that much higher doses of this drug are necessary to raise the blood pressure than occur in physiological conditions[1]. In the present experiments we investigated the action of synthetic vasopressine on the blood pressure, cardiac output and the organ fractions of the cardiac output in rats.

Methods. We used our inbred rats in pentobarbital sodium anaesthesia (40 mg/kg i.p.). Blood pressure was registered in the carotid artery with a mercury manometer, cardiac output was determined by the dye-dilution technique, employing 0.3 ml of a 0.75% solution of Evans blue i.v. The organ fractions of the cardiac output were determined by the isotope indicator fractionation method of SAPIRSTEIN[2,3] using Rb^{86}. This method offers a possibility of measuring simultaneously the flow fractions of cardiac output among the organs—except the brain—because the extraction ratios of the organs are virtually the same as the whole body. The details of the methods employed are described in preceding papers[4–6]. Vasopressine (Lysine-8-vasopressine, Sandoz[7]) was injected intraperitoneally 15–30 min before the circulatory examinations in doses of 0.01, 0.1, 1.0 U/kg. The design of any single experiment performed on the same part, was as, follows: anaesthesia, injection of vasopressine, 15–30 min later 2.5 mg heparin[7] i.v., blood pressure reading, injection of 5–10 μC Rb^{86}, i.v., 60–80 sec later dye injection for cardiac output determination. The rats were killed with i.v. injection of a saturated solution of KCl.

Results and Comments. After administration of vasopressine, the cardiac output did not change or diminished only slightly. The blood pressure raised only after the two larger doses. The increase of the total peripheral resistance was in neither group significant (Table).

The blood flow in the coronaries, bronchial vessels and the carcass did not change after vasopressine, nor did these fractions of the cardiac output. It has been reported[8–11] that vasopressine causes a decreased flow in the hepatic artery and in the portal vein of dogs and rats, and that the arterial fraction of the liver blood flow increases. We did not observe such action in our experiments (see Table), only after administration of 1.0 U/kg vasopressine there occurred a slight increase and after 0.1 U/kg a slight decrease of the hepatic arterial fraction.

The most striking observation was the significant decrease of the blood flow and increase of the circulatory resistance in the skin. This occurred also after small doses (0.01 U/kg i.p.) of vasopressine, which did not raise the blood pressure (see Table). Similarly POTTER and SUFTIN[12] observed, after a dose of vasopressine which did not alter the blood pressure, a diminished flow in the femoral artery of dogs. It appears, therefore, that the physiological action of vasopressine is not primarily concerned with the rise of the blood pressure. Considering the biological halftime of vasopressine, which is less than 1 min[13,14], and the pronounced increase of the vasopressine

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Effect of vasopressine on the circulation in the rat

		Control	1.0 U/kg i.p.	0.1 U/kg i.p.	0.01 U/kg i.p.
	Number of cases	19	13	12	10
		Mean values ± standard deviation			
Total body	Cardiac output	25.0 ± 3.9	25.9 ± 3.9	23.5 ± 5.0	21.8 ± 3.9°
	Blood pressure	113.9 ± 10.8	128.1 ± 12.0··	122.5 ± 9.7·	116.5 ± 9.2
	Resistance	380.6 ± 76.1	404.3 ± 89.5	432.6 ± 96.0	436.3 ± 73.6
Liver	Blood flow	54.5 ± 15.7	71.8 ± 22.7·	50.1 ± 9.2	44.4 ± 11.1
	Resistance	179.4 ± 54.1	155.4 ± 48.6	202.1 ± 44.1	218.9 ± 46.1
	Fraction	9.8 ± 1.8	12.0 ± 2.7·	8.7 ± 1.2··	8.4 ± 1.2
Intestine	Blood flow	66.4 ± 21.1	63.6 ± 16.6	58.5 ± 16.2	52.3 ± 10.7
	Resistance	151.8 ± 56.2	172.9 ± 56.8	177.9 ± 46.6	184.4 ± 36.5
	Fraction	17.1 ± 3.0	17.7 ± 3.5	18.4 ± 3.4	18.1 ± 2.0
Skin	Blood flow	10.3 ± 2.8	6.9 ± 2.4··	7.9 ± 2.6·	7.5 ± 1.1··
	Resistance	953.6 ± 298.6	1754.5 ± 994.9··	1349.8 ± 378.1··	1254.1 ± 176.4··
	Fraction	8.5 ± 1.6	5.7 ± 1.5···	7.4 ± 1.3	7.6 ± 0.8
Scales	Cardiac output	ml/min/100 g body weight		No symbol	$P > 0.05$
	Blood pressure	mm Hg		·	$P < 0.05$
	Resistance (body)	10^3 cm dynes sec^{-5}/100 g body weight		··	$P < 0.01$
	Blood flow (organ)	ml/min/100 g weight of organ		···	$P < 0.001$
	Resistance (organ)	10^3 cm dynes sec^{-5}/100 g weight of organ			
	Fraction	blood flow of total organ expressed in % of total cardiac output			

content of blood after bleeding[15,16], the doses of vasopressine employed in our experiments will be within the physiological limits.

After bleeding, a significant decrease of the blood flow in the skin has been observed by SAPIRSTEIN et al.[17] and by TAKÁCS et al.[18] in the rat. Possibly this phenomenon may be caused by a release of vasopressine. This hypothesis is supported by two observations: a significant increase of the vasopressine level in the blood has been observed after bleeding[15,16]; on the other hand, dogs tolerate bleeding less well after neurohypophysectomy[19].

Zusammenfassung. Vasopressin in den Blutdruck nicht erhöhenden geringen Dosen (0.01 E/kg i.p.) verringert die Hautdurchblutung der Ratte und erhöht die zirkulatorische Resistenz. In höheren Dosen von sogar 1.0, 0.1 E/kg beeinflusst Vasopressin Minutenvolumen und Zirkulation anderer Organe nicht.

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The Neurogenic Activity of High Potency Substance P

There appears to be general agreement that 'crude' substance P (SP) has an action on the nervous system[1–6]. However, there appears to be some disagreement as to whether the neurotropic action is retained with purification. Thus, STERN and HUKOVIĆ[7] have reported that as SP is purified up to 270 U/mg, it retains its ability to antagonize morphine-induced analgesia, but looses its ability to produce tranquilization. On the other hand, HAEFELY and HÜRLIMANN[8] have stated that 'purified' SP is without neurotropic activity.

This paper relates research undertaken in an attempt to determine whether the neurotropic activity of SP is lost when the material is purified to a potency of 10,000 U/mg.

Methods and Materials. In order to provide the most efficient utilization of the small amounts of SP available, the test system used was that previously described from these laboratories[6], i.e. potentiation of the fourth dorsal root potential (DR IV), by substance P in the presence of lysergic acid diethylamide (LSD).

Decerebrate cats were used in all of these experiments. Decerebration and laminectomy were performed under ether anesthesia. Dorsal root potentials (L7 or S1) were evoked at a frequency of 2.5 cps, using stimuli approximately 50% of maximal and 0.05 msec duration. Ether anesthesia was stopped at least 1 h prior to the administration of SP or LSD. No experiment was initiated until the dorsal root potentials were observed to be constant for at least 30 min.

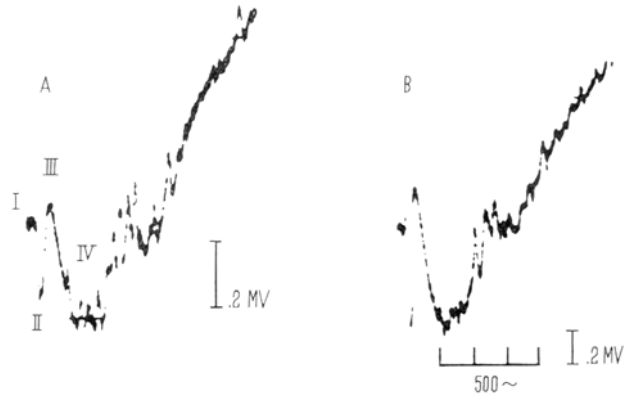
After a control period of 30 min, LSD, 20 μg/kg, was injected i.v. After a period of approximately 10 min, during which time DR IV was seen to increase in amplitude, and then to remain constant at the new level, SP was injected i.v.

The SP used in these experiments was of three potencies, 10 U/mg, 1,000 U/mg, and 10,000 U/mg[9], and was purified as described earlier[10].

Results. (1) LSD: In each instance the administration of LSD was followed by an increase in DR IV. This had been described earlier[6], and no further comment is necessary at this time.

(2) SP: The results of administration of each of the three samples of SP can be described together since the results were qualitatively similar. In each instance SP, after LSD, produced a further augmentation of DR IV. In addition, in certain instances (Figure) this was associated with an increase of the first three dorsal root potentials (i.e. DR I, II, and III). Augmentation of DR I, II, and III with larger doses of SP and presumedly consequent to augmentation of DR IV has been observed and discussed in earlier reports[6].

Using SP of a potency of 10 U/mg, augmentation was seen in three cats using doses ranging from 20–40 U/kg. Using SP of a potency of 1,000 U/mg, the phenomenon



Sample traces of records from the same experiment illustrating the actions of SP (10,000 U/mg) on the dorsal root potential of the cat. Control record (A), illustrates a typical dorsal root potential (DR I–IV) after the administration of LSD, 20 μg/kg. 6 min prior to trace B, SP, 20 U/kg, was injected. Note the change in calibration of the vertical amplifier.

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