Résumé. Chez le rat la prostaglandine E_1 augmente la consommation d'oxygène et la teneur en potassium, tandis qu'elle abaisse la teneur en sodium dans le tissu rénal et hépatique. On y a observé une corrélation entre l'effet et la dose de PGE_1 employée. Cependant dans les coupes du tissu hépathique, la PGE_1 est restée sans action. A même dose la $PGF_{2\alpha}$ a produit des effets comparables à ceux qu'on obtient avec la PGE_1. Ces résultats indiqueraient que la réponse natriurétique à la PGE_1 ne semble pas due à une inhibition de la «pompe» de sodium des cellules tubulaires, mais à une élévation du flux sanguin rénal.

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Adrenergic Mechanisms in the Cerebral Vascular Bed

From the investigations of Molnár[1,2], Mchedlishvili[3], d'Alecy and Feigl[4] and others, the existence of a neural vasomotor regulation in the cerebral vascular bed emerges as a firmly established fact. It is most likely that adrenergic fibres play a dominant role in this regulation. However, there is no clear pharmacological proof concerning the quality of the adrenergic responses of the cerebral vessels. The existence of a β-adrenergic dilator effect is especially uncertain. This study was designed to clear up the latter problems by using the specific blocking capacity of α- and β-blocking agents.

Methods. Experiments were carried out on 25 mongrel dogs (10–25 kg) lightly anaesthetized with chloralose (90–100 mg/kg). Cerebral blood flow was measured by cannulating the confluence of the sagittal and straight sinuses, with the lateral sinuses occluded, according to the method described by Rapela and Green[5]. Blood flow was determined frequently by measuring the filling time of a calibrated horizontal glass tube attached to the cannula circuit by means of a T-branch at the right atrial pressure level.

The cerebral venous outflow was continuously returned to the right jugular vein. Blood pressure was measured with a mercury manometer in the brachial artery. Occasionally the fluctuations of the blood pressure were damped by a pressure-stabilized chamber connected to one of the femoral arteries. In 8 cases, instead of venous outflow, the local tissue blood flow of the parietal cortex and/or of the subcortical white matter was recorded with the aid of the heat clearance technique using needle-shaped heated copper constantan thermocouples. Adrenaline (Tonogen, Richter) and isoprenaline (Isuprel, Winthrop) were used as adrenergic activators, while α- and β-adrenergic blockade was effected by phentolamine (Regitine, Ciba) and propranolol (Inderal, I.C.I.), respectively. The drugs were injected i.v. Heparin 500 I.U./kg was administered as an anticoagulant. The results were examined statistically using Student's t-test for paired data.

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Adrenergic responses of the cerebral vascular bed

	Mean arterial blood pressure (mmHg)		Cerebral venous outflow (ml/min)		Cerebral vascular resistance (mmHg/ml/min)	
	I. Effect of 1.0 μg/kg isoprenaline before (A) and after (B) 0.3 mg/kg propanolol administration. $n = 7$.					
	Control	Isoprenaline	Control	Isoprenaline	Control	Isoprenaline
A)	86.4 ± 10.2	72.3 ± 6.3[a]	14.7 ± 2.9	13.4 ± 3.1[a]	6.76 ± 1.26	6.88 ± 1.27[a]
B)	83.6 ± 9.0	84.8 ± 9.9[a]	15.1 ± 3.0	15.4 ± 2.9[a]	6.49 ± 1.19	6.41 ± 1.25[a]
	II. Effect of 2.0 μg/kg adrenaline before (A) and after (B) 0.3 mg/kg phentolamine administration. $n = 7$.					
	Control	Adrenaline	Control	Adrenaline	Control	Adrenaline
A)	89.9 ± 9.6	135.4 ± 14.0[b]	17.3 ± 4.2	16.6 ± 3.7[a]	6.57 ± 1.43	10.74 ± 2.55[b]
B)	74.2 ± 10.4	84.1 ± 12.8[a]	18.6 ± 3.7	20.3 ± 3.9[a]	4.41 ± 0.77	4.64 ± 0.78[a]
	III. Effect of 2.0 μg/kg adrenaline before (A) and after (B) 0.3 mg/kg propranolol administration. $n = 9$.					
	Control	Adrenaline	Control	Adrenaline	Control	Adrenaline
A)	84.7 ± 10.4	129.7 ± 7.3[d]	20.2 ± 4.7	23.3 ± 4.2[a]	5.22 ± 0.98	7.90 ± 1.87[b]
B)	82.3 ± 8.3	132.7 ± 13.4[d]	20.3 ± 2.3	25.8 ± 3.0[a]	4.62 ± 0.87	6.01 ± 0.83[b]
	IV. Effect of asphyxia of 1 min duration before (A) and after (B) propranolol administration. $n = 10$.					
	Control	Asphyxia	Control	Asphyxia	Control	Asphyxia
A)	90.2 ± 9.1	97.4 ± 14.4[a]	21.7 ± 4.1	44.8 ± 12.4[b]	5.60 ± 1.50	2.92 ± 0.32[b]
B)	83.5 ± 8.4	89.2 ± 10.7[a]	20.6 ± 2.9	37.8 ± 5.9[d]	4.70 ± 0.81	2.58 ± 0.30[c]

n = number of animals. [a] $p > 0.05$. [b] $p < 0.05$. [c] $p < 0.02$. [d] $p < 0.01$. Mean values ± S.E.

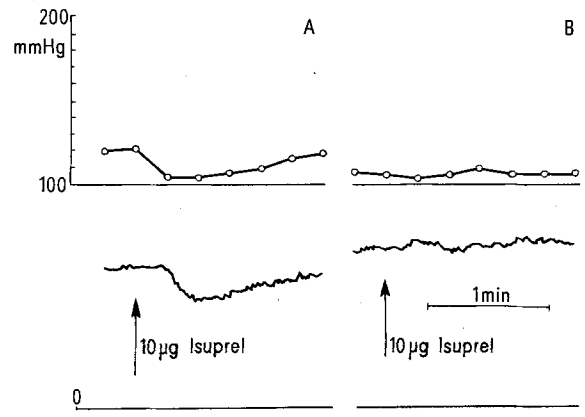

Fig. 1. Effect of isoprenaline before (A) and after (B) 0.3 mg/kg propranolol administration. 10 kg dog. Above: mean arterial blood pressure. Below: local flow of cerebral cortex.

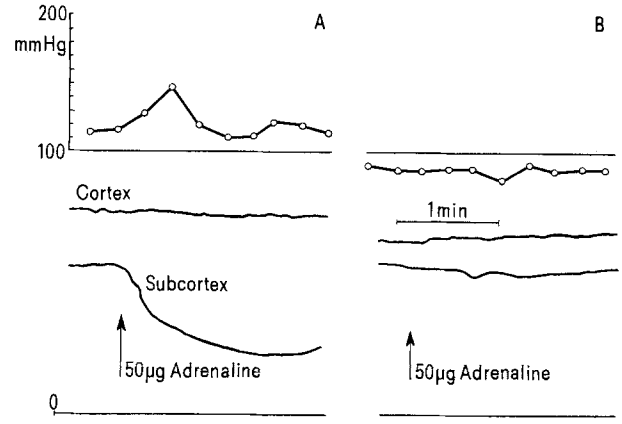

Fig. 2. Effect of adrenaline before (A) and after (B) 0.3 mg/kg phentolamine administration. 24 kg dog. From top to bottom: mean arterial blood pressure, local flow of cerebral cortex and subcortical white matter. In panel A) blood pressure increase was damped with a pressurized chamber connected to the arterial system.

Results. The results obtained by direct blood flow determinations are summarized in the Table. β-adrenergic stimulation by isoprenaline administration failed to induce any significant change in the cerebral haemodynamics (I). Adrenaline, a stimulator of both α- and β-activities induced in the cerebral vascular bed pure vasoconstriction (increase of resistance), which was completely prevented by phentolamine, an α-blocking agent (II). Phentolamine pretreatment did not reveal any masked dilator action of the adrenaline (II/B), nor was it revealed by selective for β-blockade induced by propranolol, since after the latter drug, adrenaline administration failed to elicit an accentuated increase in cerebral vascular resistance (III). Finally, β-blockade proved to be ineffective in modifying the well known enormous dilator effect of asphyxia on cerebral vasculature (IV). This excludes the possibility that β-adrenergic influences contribute to the metabolic adaptation of the vessels in the brain.

Results of the measurements of the local flow changes were consistent with the above data. Not a single experiment revealed true dilator effects after any types of adrenergic stimulation. Figure 1 shows the typical effect of isoprenaline: on administering the drug, a flow decrease ensues in the cortical grey matter, which is roughly proportional to the concommittant slight blood pressure drop. On the contrary, α-adrenergic stimulation often resulted in a regional constriction which could be abolished by α-blokade. As seen in Figure 2, there was a greater chance to obtain a clear constrictor response in the subcortical white matter than in the cortex.

Comments. On the basis of the present pharmacological analysis, the vascular bed of the brain appears to represent a typical α-region. This concept corresponds well with that recently described for the neural control of the cerebral vessels[2]. In most cases α-adrenergic constriction resulted in a mere increase of calculated vascular resistance without an appreciable flow decrease as far as the overall flow response is concerned. However, α-adrenergic stimulation does not affect the entire cerebral vascular system uniformly: by measuring local tissue heat clearance an α-sensitive decrease in flow was frequently found, especially in the subcortical regions, despite the simultaneous increase of the arterial blood pressure. In the cortex this type of response was rare. Evidently, the more pronounced metabolic demand of the cortical cells was able to mask adrenergic constriction too soon and too easily in the latter region. On the other hand, all attempts to induce beta-adrenergic dilatation in the brain proved to be unsuccessful. Moreover, as hypoxic dilatation did not change significantly after propranolol administration, β-influences could not play an important role in the metabolic adaptation of the vessels.

Zusammenfassung. Die Wirkung der Katecholamine ruft in der zerebralen Durchblutung eine Vasokonstriktion hervor, die mittels α-Blockierung behoben werden kann. β-dilatatorische Wirkung ist an den zerebralen Gefässen nicht nachweisbar.

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Effect of Some Drugs on the Chemotaxis of Rabbit Neutrophils in vitro

Introduction, There is strong evidence that cellular accumulation in inflammatory reactions is due to chemotactic and not random migration of leukocytes[1–4]. Inhibition of leukocyte chemotaxis by drugs has been studied by several workers, yielding highly diverging and not directly comparable results. The present study includes 20 drugs which could be suspected of interferring with chemotactic migration. The experimental design allows the detection of only a direct action of the drug on the cell. We have looked for neither inhibition of cytotaxin formation nor inactivation of already formed cytotaxins.

Methods. The Boyden chamber method for the in vitro evaluation of chemotaxis was used[5,6]. The cells used throughout these experiments were derived from rabbit peritoneal exudates induced by the injection of 3% sodium caseinate 2.5 h before collection and contain-