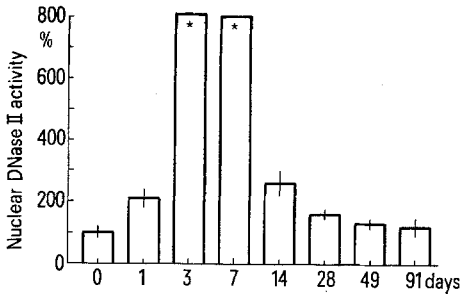

Nuclear DNase II-activity (expressed as percent of control value) of livers of rats after single p.o. administration of 210 mg/kg DENA; $n = 8$ (controls) and 2–3 (DENA-groups) resp. Control values: Protein: 3.79 ± 1.28 mg/1.0 mg DNA, DNase I: 0.029 ± 0.010, DNase II: 0.032 ± 0.006 µg DNA-P liberated/min/mg DNA. * To obtain sufficient material for preparation of nuclei, livers were pooled.

a calcium-dependent endonuclease described by HEWISH and BURGOYNE[15] remain to be elucidated.

Zusammenfassung. Durch einmalige p.o. Gabe von 210 mg/kg Diäthylnitrosamin an Ratten wurden die RNA-Konzentration sowie die DNase I-Aktivität der Leber vermindert und die DNase II-Aktivität erhöht. Die Aktivität der Zellkern-DNase II vergrösserte sich bis zum 8fachen der Norm.

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The Effect of Oxotremorine on the Acetylcholine Output from the CSF Containing Spaces

The perfusion technique was widely used for estimation of ACh output from the CNS[1], as well as for the measurement of ACh absorption from the cerebrospinal fluid (CSF)[2]. The present investigation is a study of the pharmacological possibility of influencing this output.

Materials and methods. 33 cats of both sexes weighing 2.0–4.5 kg were anaesthetized with 30 mg/kg pentobarbitone sodium (Sombital, Rafa) intravenously. Cannulas were inserted in the femoral vein to enable further injections and in the trachea to ensure ventilation.

Perfusions of the CSF containing spaces were performed in the cerebral (a) and spinal (b) CSF containing spaces. The inflow in (a) was by a modification of the FELDBERG and SHERWOOD[3] cannula, in which the tip was replaced by a 10 mm No. 18 hypodermic needle. The cannula was inserted as described by BHATTACHARYA and FELDBERG[4], but since the tip was shorter it reached about 1–3 mm above the ventricle. This cannula served as a guide for a specially prepared needle, which was inserted into the ventricle. This modification was performed to ensure proper flow. The outflow cannula was placed in the cisterna magna as described by BHATTACHARYA and FELDBERG[4]. The inflow cannula in (b) was inserted into the cisterna magna and the outflow cannula into the lumbosacral subarachnoid space as described by EDERY and LEVINGER[5].

The osmotic pressure of the artificial CSF[6] was compared to the natural CSF collected from a cannula placed in the lumbosacral subarachnoid space, using an Advanced Instruments Inc. Wide Range Osmometer. This was done in order to evaluate the effects of osmotic pressure differences of the diffusion of substances into the spaces.

The perfusion procedure was similar to that described by EDERY and LEVINGER[5], whereas the perfusion rate was kept constant at 12 ml/h. 5 mg/100 ml eserine were added to the perfusion fluid. The effluent was collected during the first 5 min and in subsequent 20 min samples into graduated test tubes containing 0.2 ml 0.3 *N* HCl. Oxotremorine (OTMN) was added either to the perfusion fluid (0.01 gr/kg/h) or administered i.v. (10 gr/kg). 2-(2,6-Xylidino)5,6-dihydro-4H-1,3-thiazinhydrochloride (Bay Va 1470) was added by i.v. injections (2 mg/cat).

The estimation of ACh in the effluent was performed, after its neutralization, on the isolated guinea-pig ileum, treated with mipafox and morphine[7].

Results and discussion. Table I shows the osmotic pressures of artificial and natural CSF. Many authors used the artificial CSF, which is isoionic to the natural CSF, under the assumption that the effect of the low protein content was negligible[8]. It is seen that the individual variations, as well as the differences between

Table I. The osmotic pressures and their means (mOSM) of subsequent samples collected from the lumbosacral subarachnoid spaces of 3 cats, compared to 4 samples of artificial CSF

Animal 1	Animal 2	Animal 3	Artificial CSF
355	385	319	336
331	338	346	346
328	342	339	342
344	328	326	332
349	330	326	
334	331	335	
336	330	346	
mean = 339	mean = 340	mean = 333	mean = 339

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samples from the same animal, are larger than the variations between 4 different artificial CSF preparations. It seems, therefore, that the artificial CSF could be used for studies of diffusion to and from the CSF. No ACh could be detected in all experiments in which eserine was not added.

Table II shows the effects of OTMN when added to the fluid during perfusion of the cerebral ventricles. The increase in ACh content without OTMN reached 168% after 2 h. However, when OTMN was added, after 45 min, it reached 610%. The values are given as percentages of the initial content so as partly to overcome the individual variations. The control values obtained with eserine are similar to those obtained with neostiqmine[9] and tetraethylpyrophosphate (TEPP)[5,10].

Table II. ACh collected (percentage of initial values) in subsequent samples of perfusion of the cerebral CSF containing spaces

Sample	a)	b)
1	100	100
2	157	187
3	157	107
		→
4	134	110
5	135	187
6	243	402
7	162	526
8	168	610

Each value represents the mean of 5 experiments. In controls (a) only eserine was added to the artificial CSF. OTMN was added in (b) to the perfusion fluid after 45 min of perfusion (arrow).

Table III. ACh collected (percentage of initial value) in subsequent samples of perfusion of spinal subarachnoid space

Sample	a)	b)	c)	d)
1/1	100	100	100	100
2/1	76	55	94	34
3/1	185	61	189	32
		→	→	→
4/1	274	53	99	46
5/1	190	602	172	969
6/1	190	434	281	803
				→
7/1	262	362	629	316
8/1	110	466	984	143

Each value represents the mean of 5 experiments. The controls (a) contained only eserine. OTMN was added (arrow) either by i.v. injections (b) or in the perfusion fluid (c), and in (d) Bay Va 1470 was injected (lower arrow) after the addition of OTMN.

Table III shows the effect of OTMN given both i.v. and in the fluid during perfusion of the spinal subarachnoid space. When only eserine was added, the increase in ACh content reached 110%. By i.v. injections of OTMN the amount of ACh increased by 466%, whereas by perfusion it increased by 984%. When Bay Va 1470 was injected 60 min after OTMN, a rapid decrease in ACh content was noted.

OTMN is known to increase ACh content in the brain. The present experiments show that the substance is also released from the nervous tissue. During perfusion, in which the OTMN comes closer to the nervous tissue, smaller amounts produced a larger increase in ACh output.

Bay Va 1470 is suggested as an inhibitor for ACh[11]. The present experiments, indeed, show that it causes a rapid decrease in ACh release from the CNS. Preliminary experiments in EEG, carried out in our laboratory, show that OTMN seems to lower the amplitude and raise the frequency, whereas Bay Va 1470 raises the amplitude and lowers the frequency. This is consistent with the amount of ACh obtained[12].

Zusammenfassung. Perfusion der Liquorräume im Nervensystem der Katze zeigte bei Zusatz von Oxotremorin eine Steigerung des Acetylcholingehaltes in der Perfusionsflüssigkeit. Die Wirkung von OTMN war bei der Verabreichung mit der Perfusionsflüssigkeit erheblich stärker als bei i.v. Injektion. Bay Va 1470 reduzierte hingegen wesentlich die Freisetzung von ACh.

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Prostaglandin Feedback Mechanism Limits Vasoconstrictor Action of Norepinephrine in Perfused Rabbit Ear

Prostaglandins (PG) are released by vasoconstrictors infused into the kidney[1–4] or into the spleen[5], and by sympathetic stimulation of renal[6] and splenic[7] nerves. PG release represents fresh biosynthesis, since it is blocked by indomethacin or by other inhibitors of PG biosynthesis[8].

It is not clear to what extent, if at all, the vascular wall participates in the generation of PG, which are detected in the outflow from organs treated with a vasoconstrictor, although a possibility of an intramural generation of PG by contracting blood vessels has been proposed[9,10].

Here we report that vasoconstriction induced by norepinephrine (NE) in the perfused rabbit ear is accompanied by a release of PGE-like substance, which attenuates the persistence of the pressor response to NE. Perfused rabbit ear, unlike perfused spleen or kidney, has little chance to produce PG from other sources than from contracting blood vessels.