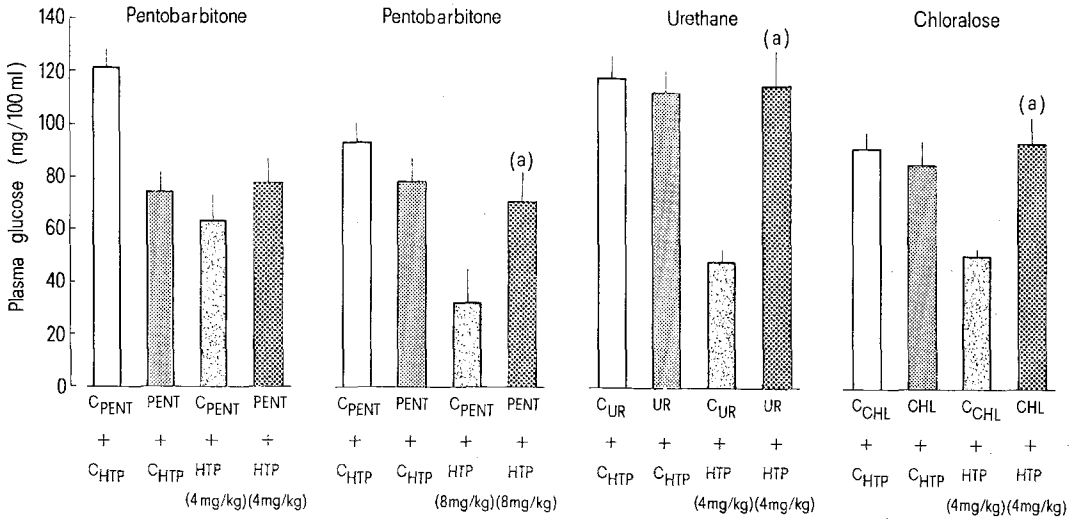

Fig. 2. Effect of pentobarbitone (PENT), urethane (UR) or chloralose (CHL) on the hypoglycaemic response to 5-hydroxytryptophan (HTP) C_{PENT}, C_{UR}, C_{CHL} and C_{HTP} refer to mice receiving the control vehicles for pentobarbitone, urethane, chloralose and 5-hydroxytryptophan respectively. Each column represents the mean of 12 observations. The vertical bars indicate the standard errors. (a) indicates a statistically significant difference ($p < 0.05$) between the plasma glucose found in mice receiving 5HTP and control vehicle for the anaesthetic (e.g. HTP + C_{PENT}), and mice receiving 5HTP and the anaesthetic (e.g. HTP + PENT).

The precise mechanisms involved in the production of hypoglycaemia by 5HTP remain to be elucidated. Furthermore, its relevance to MAOI induced hypoglycaemia as suggested by LUNDQUIST et al.[1], remains to be established.

Résumé. L'injection du 5-hydroxytryptophan par voie i.v. ou intracérébroventriculaire produit chez les souris l'hypoglycémie. Le 5-hydroxytryptamine y répond seulement lors d'une injection intracérébroventriculaire. Le 5-hydroxytryptophan n'a pas de réponse glycémique si les souris sont anesthétisées par du chloralose, de l'uréthane ou du pentobarbitone.

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Acetylcholine Output into the Liquor Spaces in Conscious Dogs

Acetylcholine release into brain of conscious animals was studied only in the cerebral cortex of rabbits and cats[1–4]. But there are no reports on the acetylcholine output into cerebral ventricles and subarachnoid spaces (liquer spaces) in animals when in a conscious state. Hence, in the present study, the magnitude of the output of acetylcholine into the cerebroventricular perfusate in unanaesthetized dogs was determined.

For this purpose a Collison's cannula and a polyvinyl tube (inner diam. 1 mm and outer diam. 2.15 mm) were placed into the left lateral ventricle[5] and into the upper cervical subarachnoid space respectively[6] in dogs of both sexes (weighing 7 to 18 kg) under pentobarbitone anaesthesia (30 mg/kg) under aseptic conditions. The next day, when the dog recovers, the cerebral ventricles were perfused with sterile artificial cerebrospinal fluid[7] at a rate of 0.1 ml/min from the cannula in the lateral ventricle to cervical cannula with the help of a palmer slow injector. The outflow fluid collected at intervals of 30 min in 0.3 ml of N/3 hydrochloric acid during perfusion, was estimated for acetylcholine-like activity within 24 h on frog rectus muscle[8] and on rat blood pressure[9,10] in albino rats[11]. The absence of stimulant action on frog rectus muscle and depressant action on rat blood pressure by the perfusate, as well as standard acetylcholine (Merck) after treatment of these preparations with D-tubocurarine (Light & Co) hydrochloride and atropine hydrochloride (Merck) respectively, confirmed the true nature of acetylcholine present in the perfusate of liquor spaces in conscious dogs. In addition, some samples in alternate experiments on assay showed the same values

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in both the preparations, and simultaneously part of these samples were made alkaline (pH 12.0) boiled and again acidified to pH 5.0 lost acetylcholine-like activity when assayed on these preparations. Standard acetylcholine solutions were made with acidified cerebrospinal fluid used for perfusion.

In a total of 285 samples, acetylcholine was found in varying amounts obtained in 25 conscious dogs. The Table shows the frequency of acetylcholine release in half-hour samples. Usually the output was between 0.1 to 1 ng/min and the next frequent range was 1 to 5 ng/min. Wide variation is seen in the ramaining samples ranging from 0.0 to 0.1 and upto 120 ng/min. Acetylcholine output was nil in 23 samples. The output varied in different dogs and from day to day in the same dog. The high values in between 20 to 120 ng/min were found in dogs on the 3rd to 4th days of perfusion. The reduced output in some dogs were found to be in a state of drowziness and during relaxation. These results are plotted in the form of a histogram in the Figure.

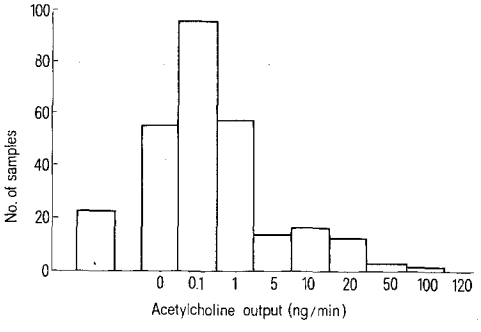
There is also a bearing on the size leading to high output of acetylcholine as seen by the values from 5 ng to 20 ng/min. Moreover, the maximum activity of the animals also showed an increase, usually from 10 to 50 ng/min and sometimes more than 100 ng/min.

This study indicates that the acetylcholine output into the liquor spaces in unanaesthetized dogs is large, since no anticholinesterase has been included in the perfusate. Another alternative is that the liquor spaces of brain have a low concentration of cholinesterase enzyme to hydrolize acetylcholine released into the perfusate. In an earlier study, we reported[6] that even 10 µg/ml eserine in the perfusate did not induce any change in the acetylcholine output into the liquor spaces in unanaesthetized dogs. The continuous perfusion might have further reduced even if low concentration of acetylcholine-esterase was present in the liquor spaces.

The source of acetylcholine present in the perfusate was from the cerebral ventricles, subarachnoid spaces around the brain stem and the upper cervical cord, since these areas are included in the perfusion system. More acetylcholine could have come from the large areas of grey matter, such as the caudate nucleus, hypothalamus and 4th ventricle, as BELESLIN et al.[12] suggested that much of acetylcholine release is from grey matter when the different parts of lateral and 3rd ventricles were perfused in cats under chloralose anaesthesia.

The frequency range of acetylcholine release into the liquor spaces of unanaesthetized dogs in 30 min ventricular perfusate samples

Serial No.	Acetylcholine output (ng/min)	Total	%
1	Nil samples	23	8.070
2	0–0.1	57	20.000
3	0.11–1.0	97	34.035
4	1.1–5.0	59	20.700
5	5.1–10.0	15	5.263
6	10.1–20.0	17	5.970
7	20.1–50.0	13	4.560
8	50.1–100.0	3	1.052
9	100.1–120.0	1	0.350



The frequency distribution of acetylcholine output in 285 half hourly perfusate samples during perfusion of liquor spaces with artificial cerebrospinal fluid in unanaesthetized dogs. The columns show number of samples in each range and the concentration of acetylcholine (ng/min) is given at its base.

Zusammenfassung. Acetylcholin kann im Liquor von wachen Hunden gemessen werden, wobei die gemessene Menge dem wachen Zustand entspricht.

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Structure-Activity Relationship of the Cardenolides Derived from Digoxigenin and Digitoxigenin, with Special Reference to the Configuration at C-5

In connection with the structure assigned to a new cardiac aglycone, syriogenin[1], 5α-digoxigenin (Ia)[2] was prepared from digoxigenin (IIa) via 3-oxodigoxigenin (IIc) and 3-oxo-Δ^4-digoxigenin (IIIa). In the course of this synthetic work, 3-epi-digoxigenin (IIe) and 3-oxo-$\Delta^{1,4}$-digoxigenin (IVa) were also obtained. Thus, the cardiotonic activities of these 6 compounds were tested by using the Straub's preparation, and compared with those of the corresponding compounds derived from digitoxigenin (IIb), namely uzarigenin (Ib), digitoxigenone (IId), Δ^4-digitoxigenone (IIIb), 3-epi-digitoxigenin (IIf), and $\Delta^{1,4}$-digitoxigenone (IVb).

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