tion of systemic hypoxia, hyperpyrexia and lactacidosis to the genesis of neuronal pathology is largely eliminated.

Materials and methods. Three female adolescent baboons (wts 3.3–3.6 kg) were anaesthetized with halothane and a carotid and femoral artery exposed to permit determination of arterial pressure, blood gas tensions and cerebral blood flow (by isotope clearance[10,11]). Needle electrodes in the scalp were used to record the EEG. Animals were given gallamine triethiodide (10–15 mg) and mechanically ventilated on air (pump volume adjusted to give moderate hyperventilation as judged by arterial Pco_2). Bicuculline (0.5–1.1 mg/kg) was given i.v. and physiological changes recorded for 4 to 8 h. Finally the brain was perfusion-fixed with formalin, acetic acid, methanol (in ratio 1:1:8) and processed histologically[8].

Results. EEG seizure activity began within 10 sec of the injection and was sustained for 3 h 25 min-3 h 45 min and, in baboon No. 706 (Figure) for more than 7 h 30 min. Arterial pressure rose immediately after seizure onset, systolic pressures transiently rising to 180–260 mm Hg. Subsequently blood pressure was midly elevated or normal. Control arterial pH showed moderate alkalosis but tended to fall throughout the seizure, so that late values were in the range 7.40–7.43. In 2 animals body temperature had fallen before seizure onset to 33.8–34° and rose during the seizure to 36.0–36.5°, in the third baboon (No. 714) temperature rose to 38.1 °C late in the seizure. Control oxygen tensions (measured on an IL polarographic analyzer model 125 A, at 37 °C and corrected to original body temperature) were in the range 75–93 mm Hg; subsequent values fell within this range except for a single value of 72 mm Hg at 4 h in No. 706. Control Pco_2 values were in the range 17–27 mm Hg; during the seizure Pco_2 rose slightly (range 23–42.5 mm Hg). Blood flow in the cerebral grey matter (calculated from the half-times of the rapid exponential component of the clearance curve) showed control values in the range 59–66 ml/100 g/min. During the seizure flow was increased 2–3 fold for up to 2 h; later values were above control values except at 7 h in No. 706 (56 ml/100 g/min compared with a control value of 61 ml/100 g/min).

Histological examination revealed, in all 3 animals, ischaemic cell change involving hippocampal neurones in the Sommer sector (particularly at the junction of h_1 with h_2; Figure A). Progression to the incrusted stage was seen in all animals but was prominent in baboon 706 (Figure B). Some neurones showed scalloping of the cytoplasmic outline, probably due to swelling of astrocytic processes. A lack of staining of Nissl substance was seen in some neurones with normal nuclei. Ischaemic cell change was also seen in occasional neurones in the endfolium and in the amygdaloid nuclei (2 animals). Some pyramidal neurones of the 3rd, 5th and 6th cortical layers, particularly in the occipital cortex, also showed ischaemic cell change. The cerebellum was normal in all 3 animals.

This pattern of cerebral pathology differs from what MELDRUM and BRIERLEY[8] have described after prolonged seizures in non-paralyzed babbons, in the lack of cerebellar damage and the greater importance of the hippocampal lesions. The most significant cause of hippocampal damage may be the excessive local discharges during the seizure. However, vascular disturbances related to the intracarotid injections may have contibuted to the lesions in the territories supplied by the internal carotid artery. The absence of cerebellar damage in these 3 animals strongly suggests that the hyperpyrexia, systemic hypoxia and late mild arterial hypotension observed in non-paralyzed animals are significant factors in the production of cerebellar epileptic pathology.

Résumé. Des états de mal, durant de 3 à 7 h 30 sont provoqués par la bicuculline chez 3 babouins adolescents, immobilisés par de la gallamine et ventilés artificiellement. La tension artérielle et le débit cérébral sont augmentés pendant la première partie de la crise et redeviennent normaux secondairement. Des lésions ischémiques sont observées dans la zone fragile de l'hippocampe (zone de Sommer) et dans le cortex mais le cervelet reste indemne.

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Effect of Sino-Aortic Denervation of the Venous Coronary Reflex in Rabbits

Increase of venous pressure in the coronary sinus of the anaesthetized dog causes reflex hypotension through vagal afferents[1–4]. This venous coronary reflex was found to be highly sensitive to general anaesthesia. The barbiturate sensitivity of the reflex is especially greater than that of the carotid sinus reflec[3]. The capricious elicitability and slight effects of the venous coronary reflex in barbiturate anaesthesia give rise to the possibility that these phenom are associated with a powerful opposing effect exerted by the classic buffer afferents on the coronary afferent input. It may be surmized that after elimination of the buffering role of the arterial baroreceptors, the veous coronary reflex could be successfully elicited even in barbiturate anaesthesia, since there is no longer occlusion of the coronary afferent input by effects through the baroreceptors converging on the same central vasomotor neurons or any opposing effect through other vasomotor neurons receiving an independent arterial baroceptor projection. The purpose of present study was to test this possibility.

Investigations were carried out on 14 adult rabbits of both sexes, lightly anaesthetized with pentobarbital. After insertion of a tracheotomy tube, artificial ventilation was maintained with room air. Both carotid sinus regions, the vagi and the aortic depressor nerves were carefully dissected free in the neck for subsequent sectioning. The chest

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Changes in blood pressure and venous coronary reflex effects after sino-aortic denervation and vagotomy

	A	B	C	D	*P*-values			
	Control	1 pair of buffer nerves sectioned	2 pairs of buffer nerves sectioned	vagus nerves sectioned	A-B	B-C	A-C	C-D
No. of animals	14	9	9	9				
Initial mean arterial	82.6 ± 5.2	96.0 ± 8.9	117.1 ± 11.4	124.8 ± 12.2	> 0.10	> 0.10	< 0.01	>0.10
blood pressure (mmHg)	(48:110)	(60:145)	(60:184)	(58:190)				
Reflex change in mean arte-	−14,3 ± 2.5	−19.1 ± 1.7	−43.6 ± 6.4	−0.8 ± 1.2	> 0.10	< 0.01	<0.001	<0.001
rial blood pressure (mmHg)	(−4:−36)	(−8:−24)	(−22:−78)	(−5:+6)				

Mean values ± SEM and range.

was opened by a transverse sternum-splitting thoracotomy in the 3rd intercostal space. Blood pressure was registered in the femoral artery by means of a mercury manometr. In order to increase the intravasal pressure in the coronary veins, a loose nylon snare was applied around the terminal part of the coronary sinus. Dissection was carried out carefully to keep to a minimum the number of nerve fibres that might be damaged. Occlusion was accomplished by pulling the thread around the coronary sinus against the flanged end of a polythene tube for 30–120 sec. This procedure causes supramaximal stimulation of the venous coronary receptors[3]; the extreme effect was tested because of the reproductbility of the stimulus. After repeated control elicitation of the venous coronary reflex, section of the major buffer nerves was carried out, either in 1 stage (5 rabbits), or in 2 stages (9 rabbits). Again, coronary reflex effects were induced. Following deafferentation, 5 animals were excluded from further experimental analysis because of great instalibities of their arterial blood pressure, The results were examined statistically using Student's *t*-test.

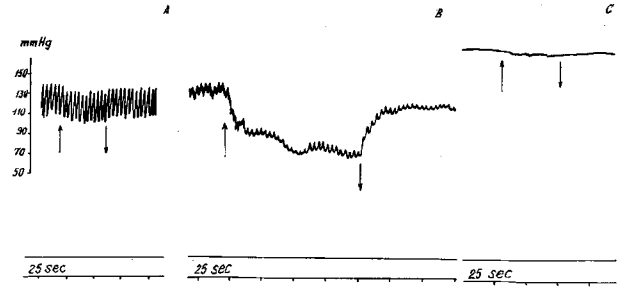

Fig. 1. Venous coronary reflex of the rabbit. Blood pressure. A) control. B) after complete sino-aortic denervation. C) After vagotomy. Between the arrows occlusion of the coronary sinus.

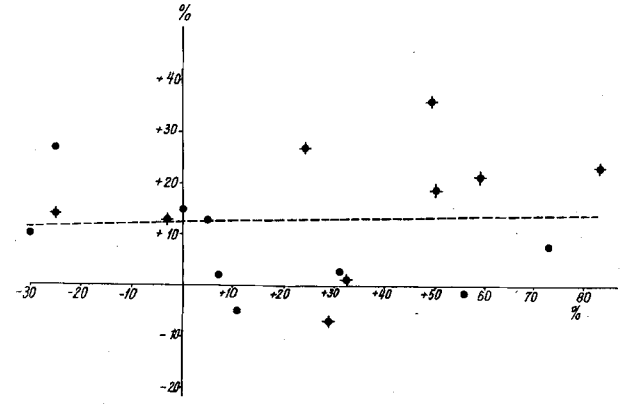

Fig. 2. Comparison of the changes in blood pressure and venous coronary reflex effects after buffer denervation. Abscisse: percent change in the initial blood pressure. Ordinate: difference in the reflex effects expressed as the percent decreases of the respective initial blood pressure levels. ●, 2 buffer nerves cut; ✦, 4 buffer nerves cut; -----, line of regression.

In the control state, the depressor effects which could be elicited by temporary occlusion of the coronary sinus were usually small in extent (Table). Section of 1 pair of the buffer nerves caused only an insignificant augmentation of the reflex blood pressure drop. In contrast, when the total buffering effect of the 4 major arterial baroreceptor areas was eliminated, depressor effects of often considerable magnitude could be induced from the venous coronary receptors (Figure 1). On the average, there was a threefold increase in the response after section of both carotid and aortic nerves. The depressor response was totally abolished by bilateral vagotomy. This substantiated earlier findings that hypotensive effect was entirely reflex[1–4].

It is known that impulses of the arterial baroreceptor fibres normally exert restricting influences on tonic sympathetic activity[5]. Consequently, in most animals with section of the carotic sinus and aortic depressor nerves, there was some resting increase of the arterial blood pressure. At the same time simultaneous augmentation of coronary reflex effects was not directly related to this hypertension. This fact is most clearly seen by comparing the changes in resting blood pressure level with the differences in depressor reflex effects obtained after partial and total buffer deafferentation (Figure 2). As can be seen, the calculated linear regression has only a negligible positive slope ($Y = 11.8 + 0.02\,X$); there is no significant correlation between the changes ($r = 0.055$ $p > 0.50$). This suggests that absence of buffering activity per se plays a more important role in potentiating the circulatory effects of the venous coronary receptors than the higher background tonic sympathetic activity brought about by buffer deafferentation. There is good reason to believe, therefore, that a true increase in the gain of the venous coronary reflex sets in after the major arterial baroreceptor influences heve been eliminated. This conclusion

is also endorsed by current concepts of the cardiovascular reflex interplay[5].

Zusammenfassung. Nachweis eines latenten reflektorischen Blutdruckabfalls bein Kaninchen in Pentobarbital-Narkose nach der Denervation des Karotis Sinus und des Aortenbogens. Die Reflexauslösung erfolgt durch Steigerung des venösen Drucks im Sinus coronarius.

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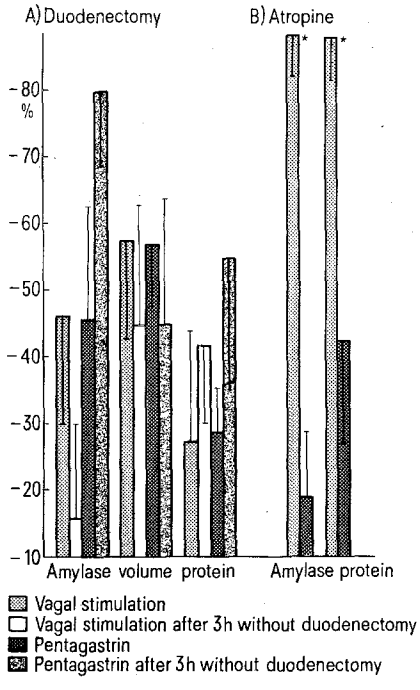
Does Vagal Stimulation Liberate Secretin and/or Cholecystokinin in Pigs?[1]

Vagal stimulation is a potent stimulator of pancreatic secretion in pigs[2]. In dogs vagal section reduces the daily output of pancreatic juice[3]. This may result from depressed sensitivity of the pancreas to the pancreatropic hormones[3] but it may be that vagi release secretin and cholecystokinin from the mucosa[4]. We have attempted to decide between these two explanations.

Material and method. Pigs were anesthetized with i.v. chloralose. The pancreatic duct was cannulated, the pylorus clamped and the lesser omentum divided so that the entire pyloric part of the stomach was deprived of its vagal supply. The stomach was drained continuously via a stomach tube passed through the mouth. I.v. secretin[5] was given throughout the experiment at a rate of 0.25 U min in 2 ml of saline. Juice was collected at 5 or 10 min intervals depending on the secretory rate.

Stimulating electrodes were placed on both vagi and major branches 3–4 cm above the diaphragm. The vagi above the electrodes were crushed and tied tightly and the animals maintained on a respirator. Stimulation was always at 25 Hz and 10 volts.



A) Percent change in amylase and protein in response to vagal stimulation or pentagastrin after duodenectomy and after 3 h without duodenectomy compared with control response before. All values significantly less than the preduodenectomy or 1 h control. B) Effect of atropine on the amylase and protein responses to vagal stimulation or pentagastrin expressed as precent decrease from pre-atropine control. * Values significantly different from pre-atropine control.

In the 5 animals the pancreatic reponses to 10 ml of 1/10 *N* HCl given intraduodenally, 10 µg gastrin pentapeptide (pentagastrin)[6], 10 µg cholecystokinin (CCK)[7] and vagal stimulation were tested as a control.

After the controls, the whole small intestine between the pyloroduodenal junction and the ligament of Treltz was removed and CCK, pentagastrin and vagal stimulation repeated as before. Two or three 10-min-periods were allowed between each procedure or enough time to allow the volume of secretion to return to basal. Animals which did not respond to HCl were discarded.

In 9 control pigs, CCK, pentagastrin and vagal stimulation were repeated at intervals for 5 h to estimate decline in response with the passage of time. In the 5 duodenectomized and 2 of the control pigs, as the last procedure, the effect of 1/10 mg of atropine/kg on vagal stimulation was tested.

In every case the responses after duodenectomy were compared with the responses in the control animals after the same time interval using the non-paired *t*-test. Responses were compared also with the mean of the previous control.

Amylase was estimated using the dinitrosalicylic acid method in the Autoanalyzer[8]. It was expressed as mg of maltose/min. Total proteolytic activity was expressed as mg of tyrosine liberated from hemoglobin substrate in 10 min[9]. Protein was measured by optical density at 280 nm and expressed as mg of bovine albumin.

Results. Duodenectomy (Figure). With the passage of time the responses of the pancreas to all of the stimuli used fell slightly. A significant reduction in the amylase, protein and protease responses to vagal stimulation followed duodenectomy. The volume response was not significantly diminished. There were similar significant and equal depressions in the responses to pentagastrin and CCK.

There was no difference between the reduction in any vagal response following duodenectomy and that seen in control animals after 3 h of experimentation whether

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