date nucleus and globus pallidum; negative results were obtained after implantation in the ventral part of the caudate nucleus, in the region medial to the caudate nucleus (N. lateralis septi), in subthalamic structures, and in the substantia nigra.

Sham implantations, made by introducing the empty cannula into the same sites, had no effect. Moreover, in the caudate nucleus of 8 animals *meta*-tyrosine was implanted; this drug has the same chemical structure as DOPA, but lacks a hydroxyl group at the *para*-position. *Meta*-tyrosine implantations did not provoke gnawing behaviour, which indicates the specificity of DOPA and apomorphine effects.

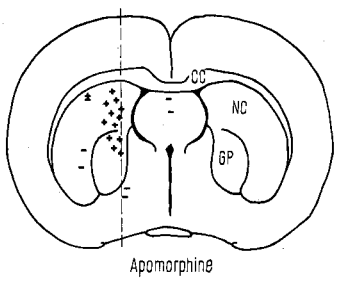

Fig. 3. Implantation sites of apomorphine, shown in frontal section, at plane indicated in Figure 2.

Conclusions. The site of action of DOPA as well as apomorphine appears to be located in the neostriatum. This indicates that accumulation of dopamine in this structure results in compulsive gnawing behaviour in rats, and that apomorphine, due to its structural relationship with dopamine, is capable of imitating this effect.

Zusammenfassung. Es wird die Relation von Struktur und Wirkung zwischen Dopamin und Apomorphin beim Zwangsnagen der Ratte, nach stereotaktischer Implantation der beiden Substanzen besprochen.

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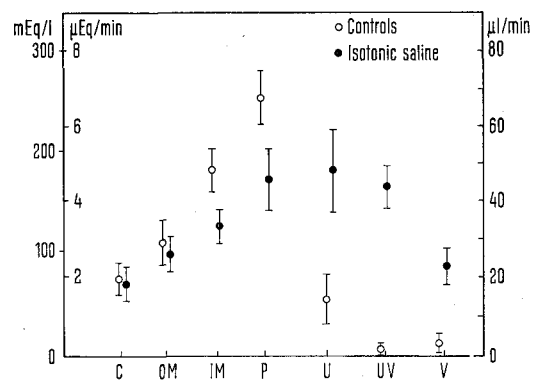
May 22, 1966.

The Composition of the Renal Medulla During Natriuresis Accompanying Saline Loading in the Rat

The expansion of the extracellular fluid volume by isotonic saline infusion is accompanied by diuresis and natriuresis. This cannot be explained by an increase of the glomerular filtration rate, because even if it is experimentally decreased, these changes take place[1]. The mineralocorticoids[1] and antidiuretic hormone[2] are also not responsible for these changes. DIRKS, CIRKSENA, and BERLINER[3] proved in dogs and CORTNEY, MYLLE, and GOTTSCHALK[4] in rats by micropuncture technique that after isotonic saline infusion a decrease in the sodium reabsorption occurs in the proximal tubule. The mechanism by which this decrease takes place is not known; an unknown humoral factor other than aldosterone is considered to be the most logical explanation. This decrease in the sodium reabsorption, even if limited to the proximal tubule only, would be sufficient to explain natriuresis and diuresis after expansion of the extracellular volume. EARLEY and FRIEDLER[2], however, submitted another possible explanation of these changes. They demonstrated in experiments in dogs that after isotonic saline infusion the renal blood flow increases with a simultaneous decrease of the PAH extraction ratio; i.e. the noncortical blood flow increases and most probably therefore also the flow rate of blood through the renal medulla. This increased medullary blood flow could lead to a washout of sodium from the medullary interstitial tissue. Passive loss of water, which occurs in the descending limb of Henle's loop, whould thus – as a result of the decrease of the hypertonicity of the medullary intersticium – be decreased and the volume of the fluid flowing into the ascending limb, from where the sodium is transported, would be increased. In addition, the sodium concentration in this fluid would be decreased and, as a result of this, the net transport of sodium out of the ascending limb would decrease. If this idea is correct, the sodium concentration in the renal medulla in animals would have to be decreased during the isotonic expansion of the extracellular fluid volume.

In 38 rats, isotonic saline infusions were carried out at a rate of 0.22 ml/min for a period of 50–70 min. There was significant diuresis and natriuresis in comparison with the control group of 18 rats which did not receive an infusion (see Figure).



Values of sodium concentration in renal tissue (mEq/l of tissue water) and in urine (U: mEq/l) and of sodium excretion (UV: µEq/min) and of urine flow (µl/min) in control (o) and in isotonic saline infused rats (•). C = renal cortex, OM = outer medulla, IM = inner medulla, P = papilla.

[1] H. E. DE WARDENER, I. H. MILLS, W. F. CLAPHAM, and C. J. HAYTER, Clin. Sci. *21*, 249 (1961).
[2] L. E. EARLEY and R. M. FRIEDLER, J. clin. Invest. *44*, 929 (1965).
[3] J. H. DIRKS, W. J. CIRKSENA, and R. W. BERLINER, J. clin. Invest. *44*, 1160 (1965).
[4] M. A. CORTNEY, M. MYLLE, W. E. LASSITER, and C. W. GOTTSCHALK, Am. J. Physiol. *209*, 1199 (1965).

The sodium concentration in 1 l of tissue water on the papilla and the inner medulla was significantly lower in the infused group than in the controls; the urea concentration changed similarly. The potassium concentration in the kidney tissue was not significantly changed. If the tissue osmolality were calculated according to the formula $2 \cdot (Na + K) +$ urea, the osmolality of the tissue of the papilla and of the inner medulla would be lower in the infused than in the control group. The calculated osmolality of the tip of the papilla was very similar to the cryoscopically measured osmolality of urine.

These results are consistent with the assumption of EARLEY and FRIEDLER that after infusion of isotonic saline a washout of sodium from the renal medulla takes place. On the other hand, it is not clear whether this occurred due to an increased flow rate of blood through the medulla or due to an increased inflow of isotonic fluid into the loop of Henle as a result of decreased sodium reabsorption in the proximal tubule, as the above quoted micropuncture experiments prove, or by a combination of both. But even a third possibility cannot be excluded: if the inhibition of the sodium reabsorption in the proximal tubule is caused by an unknown humoral factor, as some of the above-mentioned authors assume, this factor might inhibit the transport of sodium even from the ascending limb; thus also the sodium concentration in the renal medulla could decrease.

Zusammenfassung. In 38 Ratten wurde die Na- und Harnstoff-Konzentration im Gewebewasser der Nierenrinde, des Nierenmarks und der Papillenspitze nach einer Infusion von isotoner Kochsalzlösung festgestellt. Die Konzentration beider Stoffe war in der Papillenspitze und in dem Nierenmark bedeutend niedriger als bei den Kontrollratten.

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Synaptic Excitation in the Corpus Striatum Inhibited by Microelectrophoretically Administered Dopamine

Several facts point to the essential significance of dopamine (DA) for the function of the basal ganglia: The high amount of DA in caudate nucleus and the putamen[1], its occurrence in terminal structures of their nerve cells[2,3], the decrease of DA in the corpus striatum following experimentally induced degeneration of the nucleus niger[4,5], and the release of DA in the caudate nucleus after electrical stimulation of the centrum medianum and in the putamen after stimulation of the nucleus niger[6,7]. Also of importance in this context is the decrease of DA in the corpus striatum of patients with Parkinson's disease[8] and the improvement of some symptoms of this disease after application of DOPA[9]. The synopsis of these facts suggests the existence of 'dopaminergic' neurones in the corpus striatum.

From the electrophysiological point of view, an interesting contribution to this field was made by BLOOM et al.[10]. It was shown that in the cat microelectrophoretically administered DA depresses the spontaneous discharge rates of most neurones of the caudate nucleus. The effect of substances upon synaptic excitation has not been studied. This, however, was the main goal of the experiments reported here. The experiments were made on non-anaesthetized rabbits which were immobilized by Gallamine and artificially ventilated. The method for electrophoretic application of different drugs was identical with the one used earlier in different limbic structures[11,12]. Neurone discharges were recorded from the caudate nucleus and the putamen which were stereotactically approached. Intralaminar thalamic nuclei were stimulated with bipolar electrodes (2/sec stimuli, duration 0.5 msec). The tracts of the stimulating as well as the recording electrodes were controlled histologically.

Only a few neurones appeared to discharge spontaneously. By application of acid amino acids, such as glutamic or homocysteic acid, many neurones could be activated (Figure 1). In some instances, spontaneously 'silent' neurones could also be activated by electrical

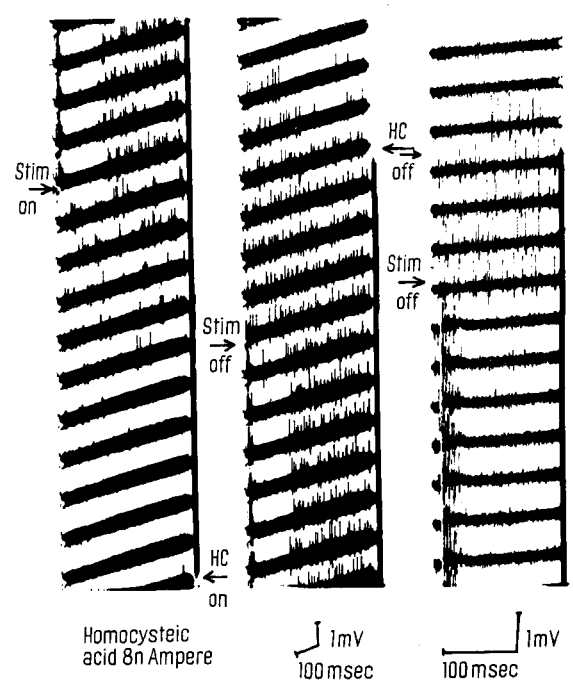

Fig. 1. Effect of homocysteic acid and combined mediothalamic stimulation upon caudate neurone discharges. Administration of homocysteic acid (HC on) produces gradually increasing activity. Electric stimulation (Stim. on) induces a characteristic response consisting of short latency discharge group (immediately following the stimulus artefact, primary activation) followed by a silent period and after-discharge. The same units are displayed with faster sweep on the right. The films are to be read from the bottom to the top.