effects in normal or in nephrectomized animals. At 50 µg/kg ouabain produced significant increases in the right ventricular contractile force, left ventricular dp/dt max, and mean arterial pressure. These effects were considerably more pronounced in nephrectomized than in normal animals, the differences were significant statistically ($p < 0.05$). Heart rate was decreased by ouabain, 50 µg/kg in normal and increased in nephrectomized dogs. In addition, experiments were performed in which ouabain was administered at 75 µg/kg i.v. to 2 normal and 2 nephrectomized dogs. At this dose ouabain produced ventricular arrhythmias in all four animals at 8 to 15 min after administration. These experiments were not used for comparative evaluation of positive inotropic and pressor effects of the glycoside.

A possibility was considered that plasma Ca^{++} levels may determine the magnitude of the positive inotropic effect of ouabain. The total plasma Ca^{++} was determined in normal and nephrectomized dogs before and after ouabain utilizing the atomic absorption spectroscopy method of WILLIS[5]. The average total plasma level in 6 normal dogs before administration of ouabain was 5.13 mEq/l with a standard deviation of 0.33. In 10 nephrectomized dogs the average total plasma Ca^{++} was 5.26 mEq/l with the standard deviation of 0.44. There was no significant difference in total plasma Ca^{++} levels in both groups of dogs. Our experiments did not exclude, however, a possibility that myocardial Ca^{++} levels may have differed in the 2 groups of animals.

The renal excretion of ouabain is not likely to account for the observed difference in the positive inotropic effects of ouabain in normal and nephrectomized dogs. Only a relatively small portion of ouabain is known to be rapidly excreted by the kidneys. The 50% excretion time for ouabain in man was estimated to be 8 h[6]. Also, a greater enhancement of the effects of ouabain at 25 µg/kg would have been expected in nephrectomized animals if the renal excretory function were responsible for the observed differences in the effects of the drug.

It is conceivable that a humoral factor of renal origin, possibly an antihypertensive substance, antagonizes not only the pressor effects of angiotensin or norepinephrine, but also the pressor and the positive inotropic effects of ouabain. After nephrectomy the absence of this factor leads to the enhancement of ouabain effects.

Zusammenfassung. In nephrectomierten Hunden erhöht Ouabain den Blutdruck und die Kontraktionskraft des Herzens mehr als in intakten anaesthesierten Tieren.

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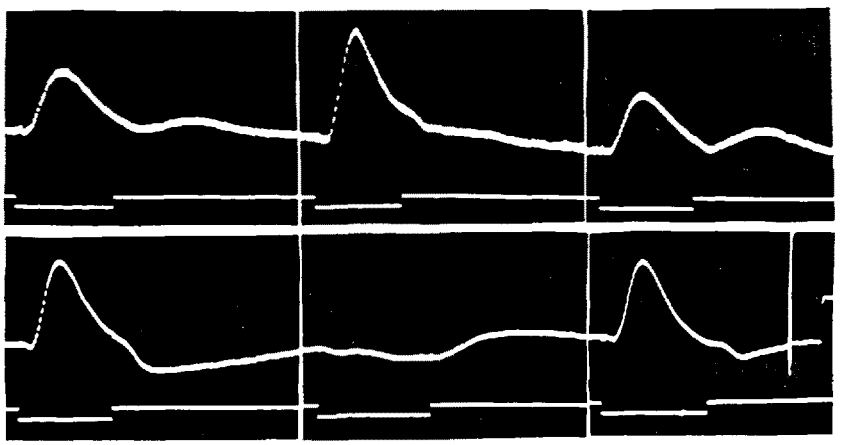
Effect of Strychnine on the Electroretinogram of the Isolated Rabbit Retina

Strychnine influences both *b*- and *d*-wave in frog[1,2]. However, no such influence could be shown as yet in ERG of rabbit and cat[3,4], although spike activity is altered in optic fibres of these animals[3,5]. From this the question arises whether strychnine may act on the second neuron of the mammalian retina and, therefore, on its ERG.

The eyes of 8 rabbits (anaesthetized by urethane 2 g/kg) were enucleated after dark adaptation of at least 1 h duration. The isolated retinae (17 preparations) were perfused by plasma saline-mixture kept at 30 °C[6] and the ERG recorded by an oscilloscope (OG2-18, VEB Messtechnik Berlin, dc-amplification).

Normal ERG of the isolated rabbit retina is shown in the Figure (upper row, left). After application of strychnine $3.5 \times 10^{-5} M/l$ the *b*-wave increases (upper row, middle). The transitory effect is reversible as shown in the right ERG (upper row). With higher concentration of strychnine ($7 \times 10^{-4} M/l$) the effect is just the opposite, the *b*-wave of the control ERG (Figure, lower row, left) practically abolished (lower row, middle). Complete restoration occurs after application of plasma-saline-mixture without strychnine (lower row, right). Strychnine in a moderate concentration ($7 \times 10^{-5} M/l$) results only in slight reduction of the *b*-wave. The dependence of the drug's effect of its concentration and of the adapta-



Influence of strychnine on the ERG of the isolated rabbit retina in concentration $3.5 \times 10^{-5} M/l$ (upper row, middle) and $7 \times 10^{-4} M/l$ (lower row, middle). Left and right ERGs are controls before and after application of strychnine to the perfusion fluid. Calibration 200 µV, light stimulus 50 mlx, approximately 1 sec.

tion state of the retina is studied in detail on the ERG of the isolated frog's retina using statistical methods[7]. For the mammalian retina the reduction of the dark adapted *b*-wave caused by strychnine-concentrations 7×10^{-5}–$7\times10^{-4}M$/l is significant with $p<0.025$ ($n=6$, $x_n-y_n\geqq19\%$ and $\leqq95\%$) tested by the sign test. The transitory increase of the *b*-wave elicited by strychnine-concentrations 3×10^{-6}–$3.5\times10^{-5}M$/l is significant with $p<0.025$ ($n=6$, $x_n-y_n\geqq10\%$ and $\leqq107\%$). In the last case the retina was slightly light adapted by repeating the stimulus every 10 or 20 sec.

The alteration of the ERGs of frog's and mammalian retina by strychnine means that strychnine already acts on the second neuron because most components of the ERG originate there[8,9]. From this the conclusion may be drawn that the effect is caused by alteration of an inhibition mechanism in the layer of the second neuron. The lack of influence of strychnine on the ERG in the experiments of WOHLZOGEN and DANIS[3,4] may perhaps be explained by the barbiturate anaesthesia of the animals in their experiments. In the clinic of strychnine intoxication, a barbiturate antagonism is known.

Zusammenfassung. Strychnin in einer Konzentration von 3×10^{-6} bis $3{,}5\times10^{-5}M$/l verursacht eine vorübergehende Vergrösserung der *b*-Welle des ERG der isolierten Kaninchennetzhaut, in einer Konzentration von 7×10^{-5} bis $7\times10^{-4}M$/l verkleinert es die *b*-Welle. Aus den Ergebnissen wird geschlossen, dass die Substanz zumindest teilweise schon auf die Schicht des zweiten Neurons wirkt.

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Autoradiographic Demonstration of Uptake and Accumulation of ^{3}H-6-Hydroxydopamine in Adrenergic Nerves

6-Hydroxydopamine (6-OH-DA) causes a long-lasting depletion of the noradrenaline (NA) content in various sympathetically innervated organs and a functional failure of transmission at the sympathetic nerve endings[1–4]. The reason for this has been shown to be due to 6-OH-DA inducing a selective degeneration of the adrenergic nerves[5–8]. Therefore this compound has attracted greatest interest above all as a denervation tool both in the central[9,10] and peripheral nervous system[8,11,12].

The mechanism by which 6-OH-DA produces its effects is not quite clear, but denervation and pharmacological experiments have disclosed that 6-OH-DA in all probability has to be taken up and accumulated in the adrenergic nerves[7,13]. In order to prove this in a more direct manner the autoradiographic localization of ^{3}H-6-OH-DA has been investigated in mouse iris after incubation of the tissue in vitro in a physiological medium containing ^{3}H-6-OH-DA.

Methods. Albino mice (N.M.R.I., 25–30 g) were used in the experiments. The mice were sacrificed under light ether anaesthesia and the irides were dissected out and transferred to incubation flasks containing Krebs-Ringer bicarbonate buffer pH 7.4 (2 ml buffer per 2 irides) with and without ^{3}H-6-OH-DA·HBr (12.4 mCi/mmole). Some irides used were sympathetically denervated by removal of the superior cervical ganglion 48 h before the experiment or by injection of 2×50 mg/kg 6-OH-DA·HCl i.v. (2 h, 16 h interval). The incubations were performed at +37 °C using a metabolic shaker.

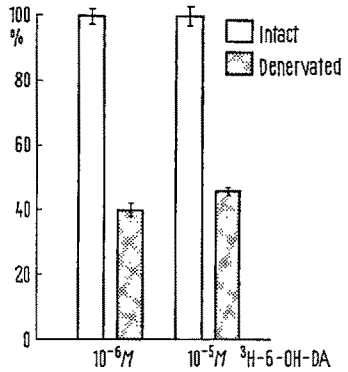

Fig. 1. In vitro uptake of ^{3}H-6-OH-DA in intact and denervated mouse irides. Each column represents the mean ± S.E.M. of 6 determinations and is expressed as percent of the radioactivity taken up and accumulated in the intact organ. Uptake in intact irides (cpm/iris): $10^{-6}M$ 141 ± 3, $10^{-5}M$ 565 ± 15.

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