

The Effect of Age and Pinealectomy on the Hypertension Produced by Adrenal Regeneration

The occurrence of hypertension during adrenal regeneration is affected by the age^{1,2} and the sex^{2,3} of the experimental animal and dependent on salt intake⁴. The cause of the higher sensitivity of infant rats to adrenal regeneration hypertension is not known, but an alteration of adrenal steroid secretion^{5,6} or a different regulation of the adrenal cortex in the pre-pubertal period⁷ could be involved. There are reports available indicating that the habenulopineal region participates in the regulation of the adrenal cortex⁸. Clearcut results in studies of epiphyseal function were obtained mostly in new-born or young animals, while in adults results were more often negative⁹. The hypertensive action of regenerating adrenal gland has a similar age dependence. It was therefore attempted to determine whether the pinealectomy affects the age dependence of adrenal regeneration hypertension.

Male Wistar-Konárovic rats, fed a pellet diet containing 0.75% NaCl, were used. Pinealectomy was performed in the new-born animals according to KINCL¹⁰ and control animals were sham-operated by opening the posterior part of the skull. At 21 and 86 days old, i.e. before and after sexual maturation unilateral adrenalectomy and nephrectomy, and enucleation of the remaining adrenal gland were performed and a 1% (w/v) NaCl-solution was substituted for drinking water¹¹. From the twenty-first to the forty-second day of the experiment (i.e. in the period of termination of adrenal regeneration), the intake of salt solution was measured. From the sixth week of the experiment, when hypertension had developed, blood pressure was measured indirectly (JELÍNEK and KRPA¹²) at fortnightly intervals. Values above 150 mm Hg were considered to be hypertensive. After termination of the experiment the animals were killed and the weight of the kidney and the dry weight of the left ventricle (prepared according to BENITZ¹³) were determined. For calculations of relative weight values, the weight of the bled body without the digestive tract was used. Student's *t*-test was used for statistical evaluation.

Mean blood pressure values (Table) were affected by pinealectomy only in animals in which hypertension was induced before sexual maturation. Values were lower in pinealectomized animals than in sham-operated controls ($P < 0.05$). Mean blood pressures were lower than in sham-operated immature rats ($P < 0.01$) and the same in both experimental and control animals made hypertensive when adult.

The intake of 1% NaCl (w/v) solution (Table) from the sixth to the twelfth week depended on the presence of the epiphysis, in a similar way as blood pressure. Peri-

natal epiphysectomy had no effect on the intake in animals exposed to SKELTON operation as adults, while the consumption of saline in animals exposed to this procedure when young is decreased ($P < 0.01$). Relative kidney weight and left ventricular dry weight in the group operated before sexual maturation were higher in sham-operated than in epiphysectomized animals ($P < 0.01$ for relative weight of the left ventricle, $P < 0.05$ respectively). In animals made hypertensive when adult, no differences were found.

The hypertensive action of regenerating adrenal gland is within limits proportional to salt intake¹⁴. The greater sensitivity of infant rats to adrenal regeneration hypertension may thus be related to the greater intake of 1% NaCl in the young¹. Also these results suggest that the greater intake of NaCl in sham-operated animals exposed to the hypertensive stimulus when young is related to higher blood pressure, while the lower salt intake in pinealectomized animals is associated with lower blood pressure and lower ventricular and kidney weights.

The pineal gland may play a role in the regulation of the electrolyte balance via the adrenal gland¹⁵⁻¹⁹ and a

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Group	Blood pressure mm Hg	Fluid consumption ml/100 g body weight/3 days	Left ventricle mg dry weight/100 g body weight	Kidney mg wet weight/100 g body weight	Body weight g
Sham pinealectomy adrenal enucleation at 21 days old	162.9 ± 6.65 (12)	107 ± 2.78 (48)	70.8 ± 2.61 (11)	904 ^a ± 25.8 (11)	270 ± 6.5 (11)
Pinealectomy, adrenal enucleation at 21 days old	143.5 ± 3.88 (16)	86 ± 2.03 (48)	62.7 ± 2.44 (16)	791 ^b ± 28.2 (15)	269 ± 7.7 (16)
Sham pinealectomy, adrenal enucleation at 86 days old	138.7 ± 1.84 (15)	62 ± 1.67 (35)	58.1 ± 1.38 (15)	669 ± 19.1 (15)	274 ± 7.2 (15)
Pinealectomy, adrenal enucleation at 86 days old	139.9 ± 1.69 (15)	62 ± 1.59 (35)	58.1 ± 0.99 (15)	643 ± 17.8 (15)	294 ± 9.0 (15)

No. of animals in brackets. ^a One values discarded because of very low body weight (154 g). ^b One values discarded because of marked hydronephrosis (1.31 mg/100 g body weight).

lower excretion of sodium was observed in pinealectomized rats than in sham operated controls²⁰. This is in accordance with the effect of pinealectomy on the salt intake, i.e. smaller losses of sodium might result in decreased intake. The appearance of that effect of pinealectomy only in animals made hypertensive before puberty suggests that the role of the pineal gland in the regulation of salt balance is lost during sexual maturation.

KINSON et al.²¹ have recently reported that pinealectomy does not effect the occurrence of renal hypertension. These authors carried out epiphysectomy in animals weighing 100 g, i.e. considerably older than in the present work. Renal hypertension was induced 13 days later, i.e. when the animals were sexually mature. Their results are to some degree in agreement with ours, for in animals exposed to the hypertensive procedure when adult we also did not observe a dependence of blood pressure on the presence of the pineal gland.

Zusammenfassung. Nach Pinealektomie unterbleibt eine Hypertonie (SKELTON), falls einseitige Nephrektomie und Adrenektomie mit Enukleation der übrigen Nebenniere bei jungen Ratten durchgeführt wurde. Wird die experimentelle, Hypertonie verursachende Operation bei adulten Tieren praktiziert, so bleibt Pinealektomie ohne jeden Effekt.

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Der Einfluss von Adrenalin auf das Verhalten des zellulären Kalziums während der K-Depolarisation des Herzmuskels von Meerschweinchen

Adrenalin kann bekanntlich die lähmende Wirkung erhöhter extrazellulärer K-Konzentrationen ($[K]_e$) am Myocard weitgehend aufheben¹. Untersuchungen über einen Zusammenhang zwischen der positiv inotropen Wirkung des Adrenalins und einer Erhöhung des transmembranen Ca-Umsatzes^{2,3} waren Anlass für die vorliegende Arbeit.

Methodik. Alle Versuche wurden an isolierten linken elektrisch gereizten (Rechteckimpulse 60/min, Impulsdauer: 1,0 msec) Meerschweinchenvorhöfen durchgeführt. Die verwendete Tyrodelösung hatte die übliche Zusammensetzung (in mM/L; KCl 2,68 bzw. 30 = K-Tyrode; NaCl 137; CaCl₂ 1,8). Die Adrenalin-Konzentration (5×10^{-6} g/ml) wurde auf Adrenalinbase bezogen. Die Kontraktionsamplituden wurden isometrisch mittels eines Dehnungsmeßstreifens (Grass FTO 3) auf einem Direktschreiber registriert. Aufarbeitung der Proben in Anlehnung an⁴. Die Aktivitätsmessungen wurden mit einem Flüssigkeitsszintillationszähler (Fa. ECKO Modell N 610 A) durchgeführt. Gleichzeitig bestimmten wir fluoreszenztrimetrisch⁵ die Ca-Konzentration. Bei der Aktivitätsbestimmung wurden die gemessenen Impulse/min (Ipm) entweder auf das Feuchtgewicht (F.G.) der Präparate (Ipm/0,1 g F.G. = Aktivität des Gewebes) oder auf den Ca-Gehalt im Gewebe (Ipm/0,1 μ Aq Ca = spezifische Aktivität) bezogen.

Ergebnisse. Die Kontraktionskraft elektrisch gereizter linker Herzohren von Meerschweinchen wird bei Erhöhung

der $[K]_e$ auf 30 mM innerhalb weniger sec bis zur völligen Lähmung abgeschwächt; diese Lähmung lässt sich durch Hinzufügen von Adrenalin zu der K-reichen Badlösung schlagartig aufheben (siehe auch¹).

Nach einer einheitlichen Äquilibrierungsphase kamen die Präparate für die Dauer von 15 min in inaktive Tyrodelösung mit einer $[K]_e$ von 30 mM, danach wurden sie in ⁴⁵Ca-haltiger K-Tyrodelösung mit Adrenalinzusatz und

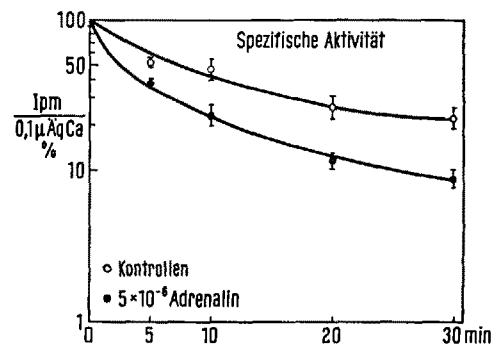


Fig. 2. ⁴⁵Ca-Abgabe aus isolierten Meerschweinchenvorhöfen unter der Einwirkung von Adrenalin und unter Kontrollbedingungen in Abhängigkeit von der Aufenthaltsdauer der Präparate in inaktiver K-Tyrodelösung. Ordinate: Impulse/min, bezogen auf den Kalzium-Gehalt des Gewebes in Prozent des Ausgangswertes der spezifischen Aktivität nach 1 h «Aufladedauer».

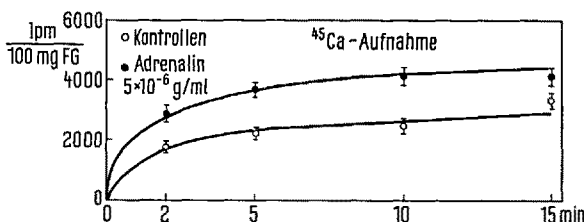


Fig. 1. ⁴⁵Ca-Aufnahme in isolierte linke Meerschweinchenvorhöfe ($[K]_e$ der Perfusionsflüssigkeit: 30 mM/L) unter der Einwirkung von Adrenalin (5×10^{-6} g/ml) und unter Kontrollbedingungen.

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