achieved, even when various manipulations, including use of layered step gradients, linear gradients of different densities, variation of centrifugation speed and when cesium chloride and potassium tartrate gradients were used. Virus particles were detected in the lower levels of the gradients, usually in the 3rd quadrant, and although sufficient quantities were not collected for nucleic acid analysis, enough were collected to determine morphological properties (figs 1 and 2). Rod-shaped virus particles in section are about 111×266 nm with an electron dense core of about 58×194 nm. Such rods form within the nuclei of midgut epithelium cells and generally acquire an envelope, composed of single or multiple layers, as they pass through the nuclear membrane[2]. Isolated rods in this study were 81×206 nm (range 71–86×180–223 nm); thus, isolated virions were similar in size to those seen in sections. Remnants of the envelope seen originally in sectioned material were also seen in isolated virions (fig. 1). Whether the envelopes are composed of nuclear membrane materials is unknown at this time. Ends of the nucleocapsids are electron dense, giving them the appearance of being capped at both ends (figs 1 and 2). Also, many rods appear to have a knob or projection at one end (fig. 2).

Morphologically, the virus particles isolated from citrus red mites are very similar to those isolated from *Oryctes rhinoceros* by Monsarrat et al.[6]. Both are non-occluded, are similar in size and structure, and are located in midgut epithelium reproducing within the nuclei. According to Matthews[7], the taxonomic status of such viruses is still uncertain, but it was proposed that they be included in the family Baculoviridae as subgroup C (non-occluded rod-shaped nuclear viruses). The Oryctes virus is the type species of the proposed subgroup, composed of virus particles with similar structure isolated from mites, Crustacea, Coleoptera and Hymenoptera.

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Intracerebroventricular angiotensin II increases arterial blood pressure in rhesus monkeys by stimulation of pituitary hormones and the sympathetic nervous system

B.A. Schölkens, W. Jung, W. Rascher, R. Dietz and D. Ganten

Hoechst AG, D-6230 Frankfurt a.M. 80 (Federal Republic of Germany), and Department of Pharmacology, University of Heidelberg, D-6900 Heidelberg (Federal Republic of Germany), 15 July 1981

Summary. Intracerebroventricular injections of angiotensin II in anesthetized rhesus monkeys increase systemic blood pressure and heart rate. These effects are accompanied by an increase in plasma ADH, cortisol, adrenaline and noradrenaline. Angiotensin II may participate in central mechanisms of blood pressure regulation by its stimulatory effect on the sympathetic nervous system, on ADH and on ACTH release in primates.

Much of what is known about the central angiotensin II (ANG II) blood pressure effects has been learned from studies in rats and dogs, in which endogenous brain ANG II has been shown to increase arterial blood pressure by the stimulation of the release of antidiuretic hormone (ADH), adrenocorticotrophic hormone (ACTH), adrenaline and noradrenaline[1–4]. Few data have been reported for primates. Neuronal fibers and cells containing ANG II-like immunoreactivity with a similar distribution to that in human brain have been identified in rhesus monkey brain[5]. ANG II injected into specific brain areas or into the ventricular system of rhesus monkeys and baboons elicits a drinking response and ADH release[6–9]. The following experiments were designed to test whether central injections of ANG II in monkeys have the same effects and to verify the concept in primates that ANG II participates in central mechanisms of blood pressure regulation. This question is important since inhibitors of the renin-angiotensin system with possibly central effects have recently been introduced for the treatment of arterial hypertension in man.

Methods and materials. ANG II was injected into the 3rd brain ventricle in sodium pentobarbital anesthetized (32 mg/kg i.p.) male rhesus monkeys (n: 5), weighing 8–10 kg; the dose was 0.5 µg/kg diluted in 25 µl artificial cerebrospinal fluid[10–12]. Systemic blood pressure was measured directly in the femoral artery using a Statham P 23Db pressure transducer. Heart rate was calculated from the ECG using a biotachometer. Blood was withdrawn from a

Effect of intracerebroventricular angiotensin II on plasma hormones of anesthetized rhesus monkeys (n: 5)

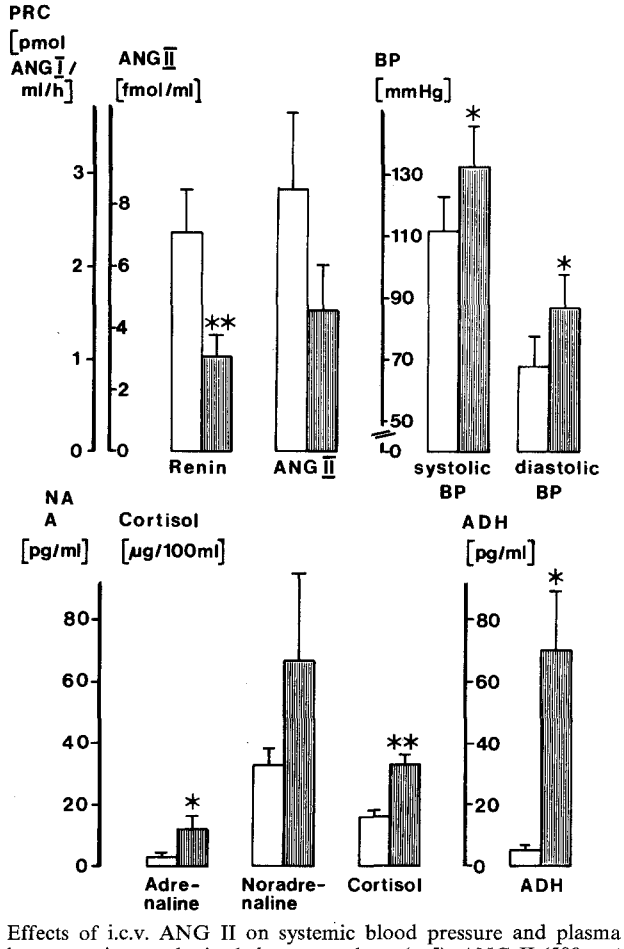
	Control	Min after i.c.v. injection of 500 ng/kg ANG II 15	60	180
Plasma renin concentration (pmoles ANG I/ml/h)	2.4±0.5	1.8± 0.4	1.2± 0.2*	1.0±0.2**
Angiotensin II (fmoles/ml)	8.5±2.5	8.2± 2.5	5.3± 2.5	4.6±1.6
Antidiuretic hormone (pg/ml)	5.0±1.5	70.5±19.1*	60.7±11.5**	22.9±3.8
Cortisol (µg/100 ml)	16.3±1.9	19.6± 3.6	25.1± 2.9**	32.9±2.9**
Adrenaline (pg/ml)	3.5±1.3	11.1± 3.6*	12.5± 2.7*	10.7±4.5
Noradrenaline (pg/ml)	33.1±5.2	67.3±28.1	50.4±13.5	34.9±5.8

Values are means±SEM. *$p < 0.05$ vs control values; **$p < 0.01$ vs control values.

femoral vein before and 15, 60 and 180 min after intracerebroventricular (i.c.v.) ANG II injection. Plasma renin concentration, ANG II, cortisol and ADH were determined by radioimmunoassays as reported[13-15]; noradrenaline and adrenaline in plasma were measured by a radioenzymatic method[16]. The position of the brain cannula was confirmed by injection of methylene blue and post mortem examination. Values are given as means ± SEM. Results were analyzed by Student's t-test. The 5% probability level was used as criterium of significance.

Results and discussion. I.c.v. injection of ANG II induced a significant increase of systemic blood pressure, which returned to initial values within 1 h. Heart rate was also increased by 6% (fig.). The cardiovascular effects were accompanied by marked changes in plasma hormones (fig.; table). Plasma renin concentration decreased by 56% and plasma ANG II by 46%. This confirms results in baboons where i.c.v. ANG II infusions reduced plasma renin activity[17]. The decreased plasma renin and ANG II concentrations following central ANG II are compatible with the notion of a negative feedback coupling between the brain RAS and the plasma RAS[3]. The concomitant increase of noradrenaline and adrenaline indicates that both the sympathoneuronal and the sympathoadrenal axis may be stimulated by central ANG II[2,18]. Plasma cortisol levels, probably due to ACTH release were increased. This confirms previous observations in rats and dogs[4,18] and is of particular interest because glucocorticoids are known to increase the sensitivity of vascular smooth muscle to vasopressor agents such as catecholamines[19]. Glucocorticoids also increase brain angiotensinogen content, which could in turn increase the central ANG II formation[20]. I.c.v. injection of ANG II equally induced a marked increase of ADH, as reported before in conscious rhesus monkeys[8]. Apart from its volume retaining effect, ADH has been proposed to be a pressor hormone[21] and to potentiate vascular effects of various vasoconstrictor agents[22]. The dependence of pressor responses elicited by i.c.v. injection of ANG II on the release of ADH has been demonstrated[23].

These findings demonstrate that centrally injected ANG II elicits the same cardiovascular and humoral responses in a primate species as in rats and dogs[2-4]. Central peptidergic stimulation has previously been shown to contribute to the establishment and maintenance of high blood pressure in experimental animals[2,18]; our results show that this possibility also exists in primates. Antihypertensive drugs which inhibit the renin-angiotensin system may thus lower blood pressure by interference with peripheral and with the central angiotensin effects[24] also in man.



Effects of i.c.v. ANG II on systemic blood pressure and plasma hormones in anesthetized rhesus monkeys (n:5). ANG II (500 ng/kg) was injected into the 3rd brain ventricle. Illustrated are the maximal responses before (open columns) and after i.c.v. ANG II (striped columns) injection; blood pressure (BP), plasma renin concentration (PRC), plasma ANG II (ANG II), noradrenaline (NA), adrenaline (A), cortisol, antidiuretic hormone (ADH). Values are means ± SEM. * $p < 0.05$ vs control values; ** $p < 0.01$ vs control values.

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