CLINESCHMIDT, B. V., PFLUEGER, A. B., BUNTING, P. R., MCGUFFIN, J. C. & BALLENTINE, R. J. (1975). *Eur. J. Pharmac.*, **32**, 279-286.

DA PRADA, M. & PLETSCHER, A. (1966). *Experientia*, **22**, 465–466.

GARRATTINI, S., BAREGGI, S. R., MARC, V., CALDERINI, G. & MORSELLI, P. L. (1974). *Eur. J. Pharmac.*, **28**, 214–216.

GLOWINSKI, J. & IVERSEN, L. L. (1966). *J. Neurochem.*, **13**, 655–669.

JUORIO, A. V., SHARMAN, D. F. & TRAJKOV, T. (1966). *Br. J. Pharmac.*, **26**, 385–392.

KELLER, H. H., BARTHOLINI, G. & PLETSCHER, A. (1973). *Eur. J. Pharmac.*, **23**, 183–186.

LAVERTY, R. & SHARMAN, D. F. (1965). *Br. J. Pharmac.*, **24**, 759–772.

MEEK, J. L. & NEFF, N. H. (1972). *Ibid.*, **45**, 435–441.

MEEK, J. L. & NEFF, N. H. (1973). *J. Pharmac. exp. Ther.*, **184**, 570–575.

PORTER, C. C., TOTARO, J. A. & BURCIN, A. (1965). *Ibid.*, **150**, 17–22.

Influence of salt and volume on changes in rat brain angiotensin

Angiotensin II has long been known to influence central nervous system function when administered exogenously. The drug can raise systemic blood pressure in dogs, alter drinking behaviour in rats, and release antidiuretic hormone (Severs & Daniels-Severs, 1973). These are pharmacological actions, the effects of large doses of angiotensin administered to the brain via an exogenous route. Of potential physiological importance is the discovery of a complete renin-angiotensin system within the central nervous system, independent of that in the periphery (Fischer-Ferraro, Nahmod & others, 1971; Ganten, Marquez-Julio & others, 1971). These workers have found brain renin to be an isoenzyme of peripheral renin, much of the angiotensin present to be in the decapeptide form (Angiotensin I), and the highest concentrations of hormone present in the hypothalamus and brainstem, the centres of cardiovascular control and salt and water regulation.

Although much anatomic work has been done, little is known about the physiology of this hormone system in the brain. One previous report has given qualitative information on possible physiological regulation (Ganten, Granger & others, 1972). This study presents quantitative data illustrating the effects of changes in sodium balance on the concentration of brain Angiotensin I.

Male Sprague-Dawley rats (250–400 g) were housed in pairs. All animals were fed standard rat pellets and had free access to tap water except where noted. Three groups were used. Control animals were untreated; one group was given meralluride (Mercuhydrin, Lakeside) (20 mg kg^{-1}, i.m.) daily and ammonium chloride (65 mg kg^{-1}, i.p.) every other day for a total of eight days. The third group was given daily injections of desoxycorticosterone acetate in oil (Dycort, Harvey) (5 mg, i.m.) on the first day and 1 mg day^{-1} thereafter for a total of eight days. These animals had free access to 0·9% NaCl.

On the day of study, animals were anaesthetized with sodium pentobarbitone (32 mg kg^{-1}, i.p.) and bilaterally nephrectomized. After a 60 min wait (sufficient to allow for the disappearance of virtually all circulating renin (Schneider, Rostorfer & Nash, 1968), decapitation and craniotomy were performed and the brainstem between the inferior colliculi and the spinal cord was removed. This tissue was quickly

Table 1. *Effects of high and low sodium regimens on brainstem Angiotensin I concentration.*

	(ng Angiotensin I g^{-1})		
	Controls	Increased Na^+ (DOCA treated)	Decreased Na^+ (diuretic treated)
mean	78·01	40·48	229·32
s.e.	0·01	6·04	54·96
P		<0·01	<0·001
n	14	6	5

washed with ice-cold 10% trichloroacetic acid saturated with 8-hydroxyquinoline SO_4 and disodium ethylenediamine tetraacetate as enzyme inhibitors. The brainstem was homogenized and the tube re-weighed. After centrifugation, the supernatants were removed, lyophilized and frozen at −20° until assay.

The amount of Angiotensin I in each sample was determined by a radioimmunoassay (Schwarz/Mann) based on the method of Haber, Koerner & others (1969). Recovery of Angiotensin I added to brainstem extracts averaged 80%. Results are expressed as nanograms of Angiotensin I g^{-1} tissue (wet weight), means ± standard error. Statistical analysis was by Student's *t*-test for group comparisons.

The mean weight of the tissue assayed was 0·164 ± 0·01 g (n = 25). The effects of the drug treatments on the concentration of Angiotensin I are shown in Table 1.

We have used a radioimmunoassay to study the effects of changing sodium and fluid balance on Angiotensin I concentration in the rat brain. The brainstem was used because of its accessibility and high concentration of Angiotensin I (Fischer-Ferraro & others, 1971). Depletion of extracellular volume and sodium with diuretics causes a large increase in the brainstem concentration of Angiotensin I, whereas volume and sodium-loading decrease this concentration. Thus, altering fluid and sodium balance causes the same directional change in brainstem Angiotensin I concentration as it does in peripheral blood via its influence on plasma renin activity. These changes may prove to be of physiological importance since, in the brain at least, Angiotensin I has been reported to act independently of conversion to Angiotensin II (Bryant & Falk, 1973).

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REFERENCES

BRYANT, R. W. & FALK, J. L. (1973). *Pharmac. Biochem. Behav.*, **1**, 469–475.

FISCHER-FERRARO, C., NAHMOD, V., GOLDSTEIN, D. & FINKIELMAN, S. (1971). *J. exp. Med.*, **133**, 353–361.

GANTEN, D.. MARQUEZ-JULIO, A., GRANGER, P., HAYDUK, K., KARSUNHY, K. P., BOUCHER, R. & GENEST, J. (1971). *Am. J. Physiol.*, **221**, 1733–1737.

GANTEN, D., GRANGER, P., GANTEN, U., BOUCHER, R. & GENEST, J. (1972). In: *Hypertension* 1972, pp. 423–432. Editors: Genest, J. and Koew, E. New York: Springer.

HABER, E., KOERNER, T., PAGE, L. B., KLIMAN, B. & PURNODE, A. (1969). *J. clin. Endocr. Metab.*, **29**, 1349–1355.

SCHNEIDER, E., ROSTORFER, H. & NASH, F. (1968). *Am. J. Physiol.*, **215**, 1115–1122.

SEVERS, W. & DANIELS-SEVERS, A. (1973). *Pharmac Rev.*, **25**, 415–449.