THE RELATIONSHIP BETWEEN DOPAMINE AND THE EXCRETION OF WATER AND SODIUM IN THE RAT

M. Akpaffiong, P.H. Redfern, B. Woodward, School of Pharmacy and Pharmacology, University of Bath, Claverton Down, Bath. BA2 7AY.

The existence of dopaminergic neurones in the kidney is now established, but the function of dopamine (DA) released from the nerves, and the mechanisms controlling DA release remains to be elucidated.

Attention has recently been drawn to the correlation between urinary Na^+ and urinary DA (Alexander et al, 1974; Ball & Lee, 1977); conversely Ball et al (1978) have shown that DA in urine can be altered independently of urinary Na^+. We have investigated the possibility that renal DA release is stimulated by an increase in renal extracellular fluid volume, irrespective of the osmolarity of the extracellular fluid.

Groups of 10 Male Wistar rats were used throughout, 6h and 24h urine samples being collected from individual animals; Na^+ and K^+ were assayed by flame photometry, and DA by fluorimetric assay after adsorption onto alumina (Anton & Sayre, 1964).

The effect of different ions on excretion patterns is shown in Table 1a. It can be seen that, as expected, each of the salt solutions produced a significant diuresis and a corresponding natriuresis. A significant correlation ($p<0.001$) between DA and both Na^+ and urine volume was observed. Only after $NaHCO_3$ was diuresis not accompanied by a measurable increase in DA, but this might be accounted for by breakdown of DA in the alkaline urine. A similar picture emerged from the administration of diuretics (Table 1b). From these results it is not possible to separate the influence of diuresis and natriuresis on DA loss. However, examination of results from water-loaded controls shows diuresis without Na^+-loss; in these animals increased urine volume was associated with increased urinary DA.

Table 1 (a) Salts	Values for 24h urine collection			
	volume (ml)	DA (nM)	Sodium (mM)	Potassium (mM)
control	8.5 ± 0.7	7.5 ± 0.02	0.93 ± 0.02	0.23 ± 0.03
NaCl 3% 20ml.kg^{-1}	12.7 ± 0.7	22.5 ± 1.5	7.44 ± 0.30	0.36 ± 0.04
KCl 3% 20ml.kg^{-1}	11.4 ± 0.3	18.0 ± 0.9	1.31 ± 0.29	0.96 ± 0.04
NH_4Cl 3% 20ml.kg^{-1}	12.3 ± 0.4	17.4 ± 0.7	2.00 ± 0.08	0.32 ± 0.16
$CaCl_2$ 3% 20ml.kg^{-1}	15.3 ± 1.1	18.3 ± 1.0	1.49 ± 0.19	0.28 ± 0.03
$NaHCO_3$ 3% 20ml.kg^{-1}	11.1 ± 0.3	8.6 ± 0.2	3.90 ± 0.18	0.39 ± 0.12
Table 1 (b) Diuretics	**Values of 6h urine collection**			
Control (20ml.kg^{-1} H_2O)	5.5 ± 0.5	3.7 ± 0.02	0.09 ± 0.02	0.15 ± 0.02
water-loaded (40ml.kg^{-1} H_2O)	10.4 ± 1.2	6.2 ± 0.3	0.09 ± 0.02	0.14 ± 0.01
Frusemide 30mg.kg^{-1}	10.2 ± 0.8	9.4 ± 0.7	0.69 ± 0.07	0.05 ± 0.09
100mg.kg^{-1}	19.7 ± 1.3	15.7 ± 1.1	0.90 ± 0.04	0.11 ± 0.05
Hydrochlorthiazide 30mg.kg^{-1}	8.0 ± 0.8	7.4 ± 0.4	0.44 ± 0.46	0.04 ± 0.02
100mg.kg^{-1}	10.4 ± 0.8	9.4 ± 0.8	0.43 ± 0.03	0.04 ± 0.01
Triamterine 30mg.kg^{-1}	7.6 ± 0.6	16.4 ± 1.5	1.12 ± 0.12	0.04 ± 0.01
100mg.kg^{-1}	12.7 ± 0.3	18.2 ± 1.2	1.69 ± 0.07	0.03 ± 0.01

In further experiments, injection of DA (10-50mg.kg^{-1} i.p.) produced a dose-dependent increase in both urine volume and urine Na^+. This, while further supporting a relationship between DA and renal function, does not help to elucidate which of these two variables is related most directly to renal DA release. A further interesting and as yet unexplained observation is that the effects of DA were blocked by chlorpromazine and by pimozide, but were potentiated by haloperidol.

Alexander, R.W. et al (1974) J. Clin. Invest. 54: 194-200
Anton, A.H., et al (1964) J. Pharmac. Exp. Ther. 145: 326-336
Ball, S.G., Lee, M.R. (1977) Clin. Sci. 43: 481-491
Ball, S.G., Oats, N.S., Lee, M.R. (1978) Clin. Sci. 55: 167-173