Evidence for Hormonal Mediation of the Renal Response to Low-Sodium Stimulation of the Brain[1] (35539)

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Ventriculo-cisternal perfusion of low-sodium artificial CSF causes large decrements in sodium excretion and increases in plasma renin activity (1). This report presents findings on the possible roles of the renal nerves and plasma antidiuretic hormone (ADH) in mediating the antinatriuresis.

Ventriculo-cisternal perfusion was performed in seven dogs, anesthetized with pentobarbital iv. Surgical preparations in these animals included: placement of stainless steel cannulas in lateral ventricle and cisterna magna; laparatomy; and cannulation of the ureter(s); cannulation of both brachial veins; and cannulation of the femoral artery. Changes in plasma ADH concentration and plasma renin activity were examined in three of these animals. In the remaining four animals, the right kidney was denervated by peeling the adventitia from the renal vessels, and cutting all visible nerves accompanying the renal artery, renal vein, and ureter.[4] To verify the extent of denervation, the fall in renal blood flow (RBF) (monitored with a square wave electromagnetic flowmeter), in response to a timed tracheal occlusion, was measured before and after this surgery. The left kidney was removed from one of the denervated animals (dog 34). Three other animals were used for evaluation of the denervation technique, but were not subjected to ventriculo-cisternal perfusion.

Clearance techniques, ventriculo-cisternal perfusion methods, blood pressure measurement, and analytical methods for sodium, potassium, creatinine, PAH, and plasma renin activity have been described earlier (1). Plasma ADH activity was measured by the method of Share and Levy (2) as modified by Bonjour and Malvin (3).

Protocol. After surgical preparation, the control solution (artificial dog CSF) (1) and the low-sodium solution (identical to control minus 25 mEq/liter of NaCl) were perfused (0.8 ml/min) from lateral ventricle to cisterna magna for alternating 50-min periods. The first control period was extended to 70–80

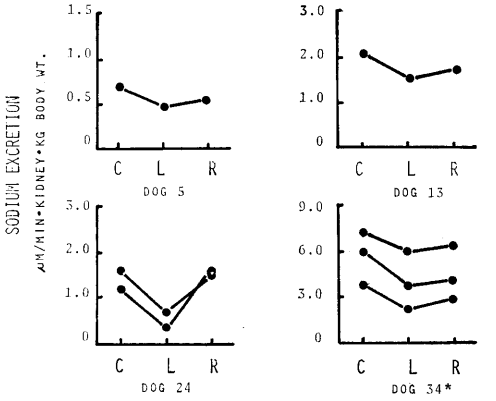

FIG. 1. Effects of low-sodium perfusion on renal sodium excretion of denervated kidneys. (C) control; (L) during low-sodium perfusion; (R) recovery. Seven low-sodium perfusions were performed in four anesthetized dogs; each line shows the effects of one low-sodium perfusion. Note that three different scales are used to accommodate the wide range of sodium excretion. * Dog 34 had the left kidney removed.

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[4] Plasma renin activity was not measured in animals following unilateral denervation without contralateral nephrectomy because, under these circumstances, plasma renin activity would reflect, primarily, renin secretion by the innervated kidney (4, 5).

min to allow an initial equilibration. Three consecutive 10-min renal clearances were performed over the final 30 min of each period and the average values for the three clearances are reported. Arterial blood samples for ADH (30–40 ml) and renin (20 ml) were taken during the final minute of each perfusion period. Blood cells were resuspended in an equal volume of 6% dextran in saline (Travenol) and were returned to the dog simultaneously with subsequent blood withdrawal; the first blood withdrawal was replaced by an equal volume of dextran in saline. Except in the denervation experiments, urinary data are for the right kidney only.

TABLE I. Effect of Hypo-osmotic Low-Sodium Ventriculo-cisternal Perfusion in Denervated Kidneys.

Seven experimental perfusions in four anesthetized dogs. All values are means ± SEM.

			Hypo-osmotic low-Na perfusion	
	n[c]	Control	During	After
1. $U_{Na}V$ (μM/min • kg of body wt)	7	3.30 ± 0.985	2.18[b] ± 0.811	2.66[a] ± 0.773
2. U_KV (μM/min • kg of body wt)	7	3.06 ± 0.601	2.67[a] ± 0.543	2.85 ± 0.594
3. Urine flow (μl/min • kg of body wt)	7	18.8 ± 5.47	14.5 ± 3.96	15.7 ± 4.59
4. ERPF (ml/min • kg of body wt)	7	7.76 ± 0.575	7.76 ± 0.525	7.83 ± 0.555
5. GFR (ml/min • kg of body wt)	7	2.73 ± 0.099	2.63 ± 0.154	2.73 ± 0.190
6. Filtration fraction (%)[d]	7	35.3 ± 2.84	35.1 ± 3.45	38.3 ± 4.16
7. Plasma Na conc (mM/liter)	7	144.9 ± 1.58	143.5 ± 0.90	143.1 ± 1.08
8. Hematocrit	5	47.8 ± 2.00	48.2 ± 2.23	47.8 ± 2.41
9. Mean arterial blood pressure (mm Hg)	7	117.0 ± 7.38	114.3 ± 8.31	114.0 ± 7.93
10. Pulse pressure (mm Hg)	6	47.9 ± 3.93	47.8 ± 4.01	47.7 ± 3.26
11. Heart rate (beats/min)	6	151.5 ± 8.12	160.2 ± 8.09	156 ± 7.01
Contralateral, innervated kidney				
12. $U_{Na}V$ (μM/min • kg of body wt)[e]	4	0.47	0.17	0.44
13. U_KV (μM/min • kg of body wt)[e]	4	1.47	0.77	1.09

[a] ($p < .05$) and [b] ($p < .01$) indicate that a given variable has changed significantly compared with the value during the previous 50-min period (next column to the left in the table); statistical tests done by paired-samples analysis.

[c] n is the number of low-sodium perfusions for which the variable is measured; all variables were not measured in all experiments.

[d] Filtration fraction calculated as GFR/ERPF.

[e] The data on innervated kidneys are from four low-sodium perfusions in three dogs; one of the four dogs with a denervated right kidney had the left (innervated) kidney removed. No statistical analysis was performed on the data from the innervated kidneys, due to the small number of experiments.

Results. Reflex renal vasoconstriction due to tracheal occlusion was decreased by denervation from a 45.2% reduction in RBF to a 4.9% reduction ($p<0.005$, $n = 7$). Low-sodium perfusion decreased sodium excretion by the denervated kidneys in each of four animals (Fig. 1); the mean decrease for seven trials was 40.7% (Table I). During the recovery period, sodium excretion returned toward control values. The contralateral (innervated kidney) was characterized by a very low control sodium excretion (Table I), which decreased by at least one-third in each of four trials; the mean decrease was 64%. Absence of the innervated kidney (dog 34) had no significant effect on the antinatriuresis (Fig. 1). Renal hemodynamics were not altered by the low-sodium perfusion (Table I).

No consistent change in plasma ADH concentration accompanied the changes in sodium excretion which occurred during the low-sodium or recovery periods. Low-sodium perfusion decreased sodium excretion in all three dogs, while plasma ADH concentration either increased, decreased, or did not change

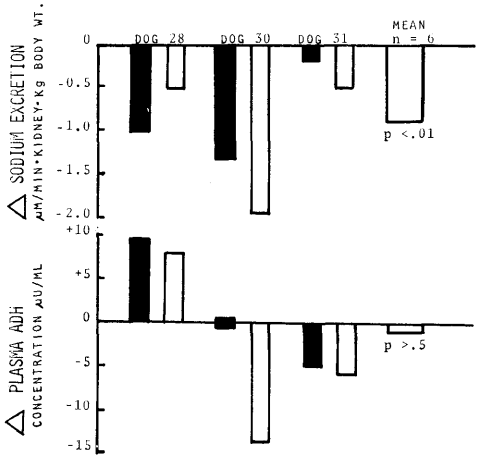

FIG. 2. Effects of low-sodium perfusion on renal sodium excretion and plasma ADH concentration. Three low-sodium perfusions were performed in three anesthestized dogs. Bars indicate sodium excretion or ADH concentration during low-sodium perfusion minus that during the corresponding control period. Mean control sodium excretion was 1.4 μM/min·kidney·kg of body wt. (solid bars) compare low-sodium to the initial control period; (open bars) compare low-sodium to the second (recovery) control period. p values indicate probability that mean is different from zero.

(Fig. 2, solid bars); sodium excretion reverted toward control values during the recovery period (control perfusion) while changes in ADH concentration were again variable (Fig. 2, open bars). Plasma renin activity increased during low-sodium perfusion (to 144, 161, and 181% of control for the three animals) without significant changes in GFR, ERPF, or systemic blood pressure, confirming earlier findings (1).

Discussion. The acute denervation was complete or nearly complete as manifested by the virtual elimination of the vasoconstrictor response to tracheal occlusion; yet sodium excretion by the denervated kidney fell during all seven low-sodium perfusions. The percentage decreases in sodium excretion were similar for innervated and denervated kidneys; the absolute decreases in sodium excretion were actually larger for the denervated kidneys. It has been previously shown that the degree of antinatriuresis produced by low-sodium perfusion varies with control sodium excretion (1). Thus, the different magnitude of the response in innervated and denervated kidneys was probably due to the greater control sodium excretion of denervated kidneys (6–8). Since removal of the innervated kidney did not significantly affect the response, it is unlikely that sympathetically mediated changes in the function (*e.g.*, changes in renin secretion) of the innervated kidney caused the response. These results indicate that the renal nerves play no important role in mediating the antinatriuresis.

Although sodium excretion was consistently reduced during low-sodium perfusion, plasma ADH concentration was increased, decreased, or unchanged. It is therefore also unlikely that ADH mediates the antinatriuresis. The mean value of plasma ADH during control perfusion (16.8 ± 2.64 (SE) μU/ml) was high and the changes were usually large compared to the sensitivity of the method (3). It is probable that abdominal surgery combined with pentobarbitol anesthesia caused both the high levels of plasma ADH activity (3) and the failure to observe the consistent decrements in ADH concentration which one might expect to result from the hypo-osmolality of the low-sodium perfusate (9).

We conclude that a hormone other than ADH mediates the effects of low-sodium ventriculo-cisternal perfusion on renal sodium excretion. The rapid onset and decay of the antinatriuresis, and the simultaneous reduction of potassium excretion [Table I and Ref. (1)] both suggest that the hormone involved is not aldosterone(10).

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