Pharmacology Biochemistry & Behavior, Vol. 40, pp. 163–168. © Pergamon Press plc, 1991. Printed in the U.S.A. 0091-3057/91 $3.00 + .00

Effect of Capsaicin Neonatal Treatment on the Salt Intake of the Adult Rat

MAURIZIO MASSI,* CARLO POLIDORI,* MARINA PERFUMI,* ROBERTO CICCOCIOPPO,* GIUSEPPE DE CARO,* CARLA BACCIARELLI† AND STEFANO MANZINI†

**Institute of Pharmacology, University of Camerino, Via Scalzino 5, 62032 Camerino (MC), Italy and †Department of Pharmacology, Malesci Pharmaceuticals, Via Porpora 22, 50144 Firenze, Italy*

Received 22 January 1991

MASSI, M., C. POLIDORI, M. PERFUMI, R. CICCOCIOPPO, G. DE CARO, C. BACCIARELLI AND S. MANZINI. *Effect of capsaicin neonatal treatment on the salt intake of the adult rat.* PHARMACOL BIOCHEM BEHAV **40**(1) 163–168, 1991.— The present study investigated the involvement of capsaicin-sensitive sensory neurons on salt intake control in the rat, following capsaicin neonatal treatment. Capsaicin did not affect salt appetite induced by intramuscular injection of deoxycorticosterone enantate, or by intracranial injection of renin. Moreover, it did not alter salt preference of rats given access to a variety of NaCl concentrations, or the need-free salt intake of multidepleted male rats. On the other hand, in response to furosemide-induced sodium depletion, the salt intake of capsaicin-treated rats was lower than that of controls. However, furosemide-induced Na^+ excretion of capsaicin-treated rats proved to be lower than that of controls, thus suggesting that difference in salt intake might be secondary to lower sensitivity of capsaicin-treated rats to the natriuretic action of furosemide. Salt intake is known to be influenced by sensory information from the oral cavity, from the liver and from the intravascular compartment. The absence of effect of capsaicin neonatal treatment suggests that sensory fibers relevant to salt intake control may not be capsaicin sensitive. On the other hand, our findings indicate that capsaicin treatment alters the renal response to furosemide and stimulate further studies on the effects of capsaicin on renal function.

Capsaicin Salt appetite Furosemide Sodium excretion Urine volume

CAPSAICIN, the pungent constituent of some red peppers of the genus Capsicum, is commonly used as a neurotoxin to elucidate the function of primary sensory afferent neurons (3). Capsaicin stimulates the peripheral endings of certain primary afferents, resulting in sensory impulse generation and local transmitter release (16, 28, 29). Shortly after its stimulating action, the sensory fibers become inexcitable by capsaicin itself and, following administration of high concentrations of the drug, also by other chemical and physical stimuli. This phenomenon, the so-called capsaicin "desensitization," involves blockade of both sensory and efferent function without degenerative changes in nerve fibers, and at high doses it is accompanied (hours–days after capsaicin challenge) by depletion of neuropeptides, such as substance P, neurokinin A and calcitonin gene-related peptide, from peripheral stores of sensory neurons (16, 17, 28, 29). Finally, neonatal capsaicin treatment in the rat is known to produce degeneration of neuropeptides-containing capsaicin-sensitive sensory nerves (25).

In relation to our interest in the study of the neural mechanisms controlling salt appetite, we thought it interesting to evaluate the effect of neonatal capsaicin treatment on the control of salt intake in the adult rat. Three main reasons have stimulated the present study: a) It is well established that sensory information from the periphery (oral cavity, liver, intravascular compartment) contributes to the arousal and to the satiation of the appetite, but it is presently unknown whether it is mediated by capsaicin-sensitive sensory neurons (2, 4, 5, 11, 12, 14, 30, 32); b) A recent study has shown that capsaicin treatment in neonatal rats enhances the intensity of deoxycorticosterone (DOC)/salt-induced hypertension. Since this experimental model of hypertension is heavily dependent on salt intake, the question arises whether the enhanced hypertension of capsaicin-treated rats might be secondary to capsaicin influence on salt intake control (18); and c) Our previous studies have shown that tachykinin peptides, which are present in capsaicin-sensitive sensory neurons, exert a potent antinatriorexic action acting in the forebrain of the rat (19–23), but it is still unknown whether they might contribute to salt intake control also as sensory neurotransmitters in peripheral sensory nerves.

METHOD

Animals

Pregnant Wistar-Nossan female rats were housed in the animal care unit at least one week before parturition. On days 1–2 of life, neonatal rats received in the dorsal thoracic region capsaicin (50 mg/kg b.wt., subcutaneously; SC) or the vehicle (10% ethanol, 10% Tween 80 and 80% isotonic saline). The injection volume was 3 μl/g. After 4 weeks, male and female rats were divided and housed 4–5 to a cage with food and water ad lib. Validity of capsaicin treatment was checked by evaluating the loss of the wiping reflex to capsaicin (0.01%) instillation into the eye. Experiments were performed in 2–4-month-old rats.

Adult rats were individually housed in a temperature-con-

trolled room on a 12:12-h light-dark cycle. Food pellets (MILL, Morini, Reggio Emilia, Italy) and water (in graduated drinking tubes) were available ad lib except when noted. Sodium chloride (NaCl) solution at different concentrations was offered according to the modalities reported in the experimental procedure.

Drugs

The following drugs were used: 1) capsaicin (ICN Pharmaceuticals, Plainview, NY), 2) DOC enantate (Cortiron; Schering, Milan, Italy), 3) furosemide (Lasix; Hoechst, Milan, Italy) and 4) renin, which was a generous gift of Prof. Detlev Ganten of the German Institute for High Blood Pressure Research. It was their preparation E III, which is purified from hog kidney by affinity chromatography (9).

Intracranial Surgery

The rats employed for renin experiments were anaesthetized (Equithesin, 3 ml/kg b.wt.; intraperitoneally) and fitted by stereotaxic surgery with a stainless steel guide cannula (o.d. 600 μ) aimed at the anteroventral third ventricle. The guide cannula was attached to the skull by stainless steel screws and dental acrylic cement. Animals were allowed one week to recover from surgery before testing began.

Experimental Procedures

Experiment 1: DOC-induced salt appetite. In relation to the questions raised by the previously mentioned study (18), DOC-induced salt appetite was the first model employed. Salt appetite was elicited by an intramuscular (IM) injection of DOC enantate 25 mg/kg b.wt., both in capsaicin-treated and in control rats. Animals had continuous access to food pellets and tap water, while 2% NaCl was offered 2 h/day, between 1100 and 1300 h. Salt intake in the 2-h test was measured for a period of 7 days following the IM DOC injection.

Experiment 2: Renin-induced salt appetite. Renin, 200 ng/rat, was given by pulse intracerebroventricular (ICV) injection in a volume of 2 μl of isotonic saline. Animals were tested three times with the same renin treatment at intervals of 7 days. Immediately before the injection of renin, 2% NaCl was removed from the cage, but water and food pellets were freely available. One h after the injection of renin, rats were given access to 2% NaCl. This time schedule was adopted so that access to salt was given when salt appetite was usually expressed in every rat. Salt intake was measured over a 2-h period of observation.

Experiment 3: Sodium-depletion-induced salt appetite. Salt appetite was elicited by an adaptation of the method of Wolf (31), in which depletion is produced by combining pharmacological natriuresis with sodium-deficient diet. Natriuresis was produced by SC injection of furosemide (Lasix; 2 injections of 5 mg/rat, separated by 2 h). At the time of the first injection, the pellets were replaced by sodium-deficient pellets (Altromin-Rieper, cod. DP/1036, Vandoies, Bz, Italy), NaCl solution was removed from the cages, and cages were washed to remove adherent salt. The animals were not deprived of water. Twenty-two to 24 h later, they were offered access to salt. Consumption of NaCl solution and water, as well as latency to drink each solution, were recorded at 15, 30, 60, 90 and 120 min. Each animal received 5 depletions at intervals of 7 days. Following the first 2 depletions, they were offered 3% NaCl; owing to the rather small intake of the solution (both controls and capsaicin-treated rats) in the following 3 depletions they had access to 2% NaCl.

Experiment 4: Need-free salt intake. Rats with a history of repeated sodium depletions are known to show an elevated daily salt intake (26). In response to the first 3 sodium depletions, rats show an escalation of their daily salt intake to higher levels that remain elevated for months and probably for the life of the animals. This intake, which is markedly more pronounced in female than in male rats, is referred to as "need-free," because it occurs in rats that have continuous access to sodium-rich pellets and it is not secondary to renal sodium loss (8).

Between depletions, salt intake of the male rats employed in Experiment 3 was daily recorded to evaluate whether the neonatal capsaicin treatment might influence their "need-free" salt intake. As stated in Experiment 3, these rats had 3% NaCl available following the first 2 depletions, and 2% NaCl after the subsequent depletions. Moreover, they had free access to tap water and food pellets.

Experiment 5: Salt preference. Salt preference was assessed by offering animals a choice between two bottles, one with distilled water and the other containing NaCl. Concentrations of NaCl (6.13, 25, 100, 200, 300 and 400 mM) were presented in ascending order on consecutive days (24). Solutions were prepared each day with reagent-grade NaCl in distilled water. Position of bottle presentation on the animal cage was alternated daily to avoid position preference. Food intake, body weight and total fluid consumption were measured daily. Solution preference was calculated by dividing the amount of NaCl solution consumed by the total fluid intake.

Experiment 6: Urine excretion following furosemide treatment. The different salt intake in response to furosemide-induced natriuresis between capsaicin-pretreated and control rats prompted us to investigate whether it might be secondary to differences in the renal responses to furosemide. Rats were put in metabolic cages so that urine spontaneously voided could be collected at different time intervals. They received the same furosemide treatment reported in Experiment 3, that is, 2 SC injections of 5 mg of furosemide, separated by 2 h. Urine was collected at 2, 4 and 24 h after the first furosemide injection. Sodium and potassium urine concentrations were determined by flame photometer (Digiflame compact, GIO.DE VITA, Rome, Italy).

Validation of the ICV injections. The ICV injection into the third ventricle of renin-treated rats was firstly validated behaviorally by checking the dipsogenic response to the ICV injection of angiotensin II (10 ng/rat in 1 μl of isotonic saline). Only animals that drank more than 5 ml in 15 min were employed in the following experiments. After completion of the experiments, rats were given an ICV injection of 1 μl of India ink and immediately afterwards, they were sacrificed with an overdose of anaesthetic. Diffusion of the dye into the brain ventricle was carefully evaluated.

Statistical analysis. Data are presented as means ± S.E.M. Statistical analysis of data was performed by split-plot multifactorial analysis of variance with between-groups comparisons for neonatal pretreatment and within-groups comparisons for time (and salt concentration in preference tests). Planned pairwise comparisons were made by means of *t*-tests. Statistical significance was set at $p<0.05$.

RESULTS

Experiment 1: DOC-Induced Salt Appetite

As shown in Fig. 1, in response to the IM administration of DOC enantate, 25 mg/kg b.wt., the cumulative 2% NaCl intake progressively increased in the 2-h test, both in controls and in

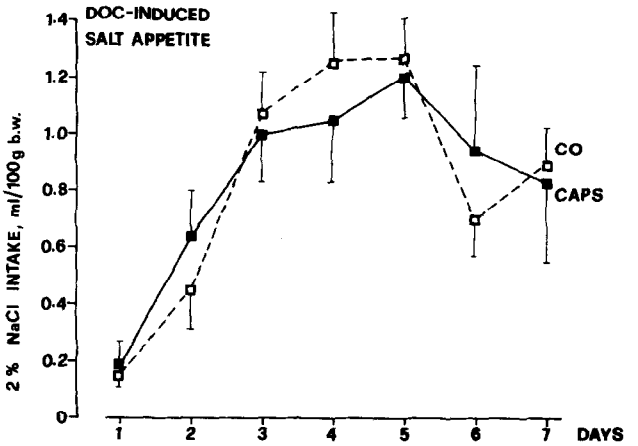

FIG. 1. Daily salt intake following DOC enantate administration in capsaicin-treated (CAPS) and in control rats (CO). Each value is the mean ± S.E.M. of 8 subjects. Difference from controls was never statistically significant.

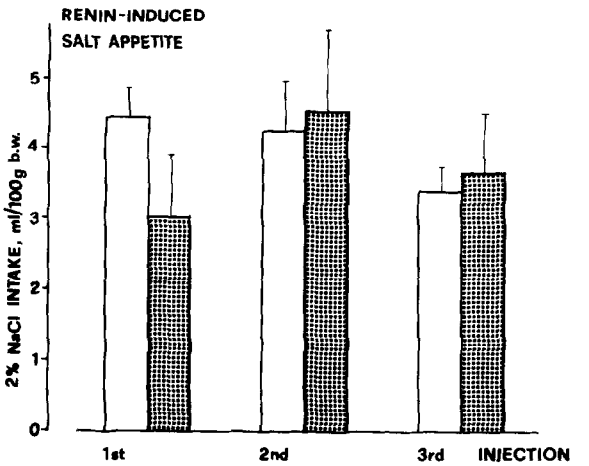

FIG. 2. Salt intake of controls (open bars) and of capsaicin-treated rats (dotted bars) following subsequent intracranial renin injections. Each value, determined at 2 h after renin injection, is the mean ± S.E.M. of 6 subjects. Difference from controls was never statistically significant.

capsaicin-treated rats, and reached a maximum at 5 days after DOC injection.

During the 7-day observation period, the salt intake of capsaicin-treated rats was strictly similar to that of control rats at the different times of observation (15, 30, 60 and 120 min after access to salt). The analysis of variance revealed the absence of effect for the neonatal treatment, $F(1,14)=0.048$, $p>0.05$, in the absence of interaction for treatment-day and treatment-time of observation.

Experiment 2: Renin-Induced Salt Appetite

Also in response to the ICV administration of renin, 200 ng/rat, the intake of capsaicin-treated rats was similar to that of control rats for each of the 3 injections (Fig. 2).

The analysis of variance revealed the absence of neonatal treatment effect, $F(1,10)=0.001$, $p>0.05$, as well as no interaction between either neonatal treatment and injection or neonatal treatment and time of observation.

Experiment 3: Sodium-Depletion-Induced Salt Appetite

The results of this experiment are presented in Fig. 3.

Following the first sodium depletion, the intake of 3% NaCl of capsaicin-treated rats was lower than that of controls during the entire 2-h period of observation. At the end of the 2-h test, the cumulative intake of capsaicin-treated rats was 58.45% of that of controls; however, the analysis of variance revealed the absence of neonatal treatment effect, $F(1,14)=1.452$, $p>0.05$, with no time-treatment interaction.

In response to the second sodium depletion, the intake of 3% NaCl of capsaicin-treated rats was again lower than that of controls. The difference between the two experimental groups proved to be statistically significant, $F(1,14)=8.458$, $p<0.05$.

In the following three depletions, when NaCl was offered at the concentration of 2%, the intake of capsaicin-treated rats was again significantly lower than that of controls, $F(1,14)=11.480$, $p<0.01$, $F(1,14)=7.001$, $p<0.05$, and $F(1,14)=11.162$, $p<0.01$, respectively.

Experiment 4: Need-Free Salt Intake

The 24-h need-free salt intake, in between the different sodium depletions, was similar for capsaicin-treated and control rats, as shown in Fig. 4.

Accordingly, the analysis of variance for each interdepletion interval revealed the absence of neonatal treatment effect.

Experiment 5: Salt Preference

As shown in Fig. 5, salt preference of capsaicin-treated rats,

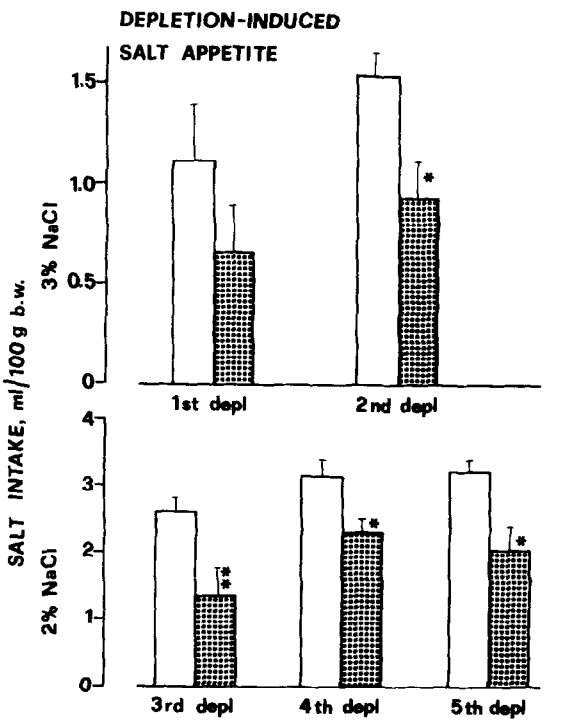

FIG. 3. Salt intake of controls (open bars) and of capsaicin-treated rats (dotted bars) following subsequent furosemide-induced sodium depletions. Values, determined at 2 h after access to salt, are means ± S.E.M. of 8 subjects. Difference from controls: $*p<0.05$; $**p<0.01$; where not indicated, difference from controls was not statistically significant.

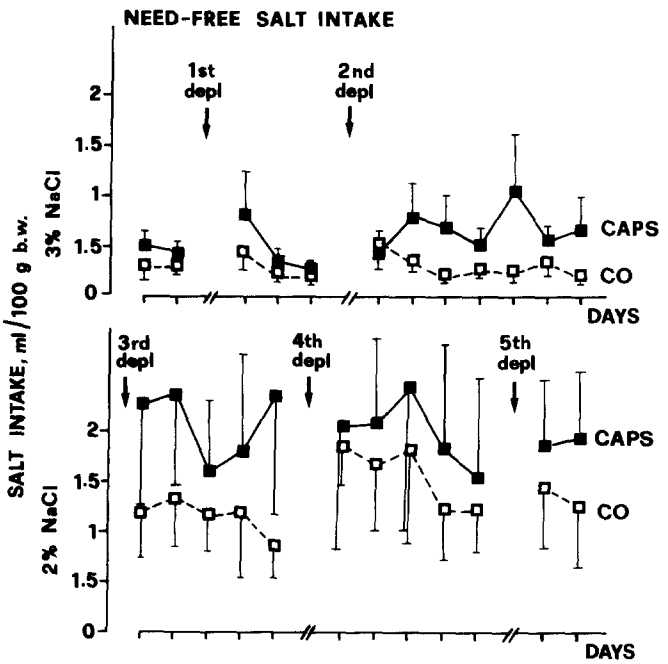

FIG. 4. Daily need-free salt intake of capsaicin-treated (CAPS) and of control rats (CO) following repeated sodium depletions. Each value is the mean ± S.E.M. of 8 data. Difference from controls was never statistically significant.

in the range of the salt concentrations tested, proved to be strictly similar to that of control rats.

The analysis of variance revealed the absence of neonatal treatment effect, $F(1,13)=0.107$, $p>0.05$, in the absence of neonatal treatment-NaCl concentration interaction.

Experiment 6: Urine Excretion Following Furosemide Treatment

Since difference in salt intake between the 2 experimental groups was detected only following furosemide-induced sodium depletion, we thought it interesting to evaluate whether it might be accounted for by a different sensitivity of the 2 groups to the natriuretic action of furosemide.

As shown in Fig. 6, the results of this experiment showed

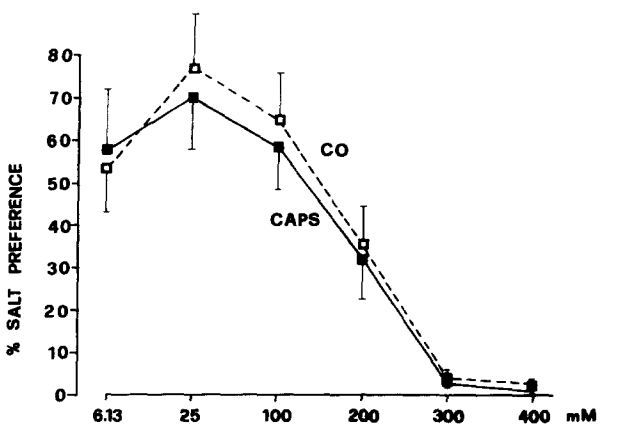

FIG. 5. Percent salt preference of capsaicin-treated (CAPS) and of control rats (CO). Values are means ± S.E.M. of 7 controls and of 8 capsaicin-treated rats. Difference from controls was never statistically significant.

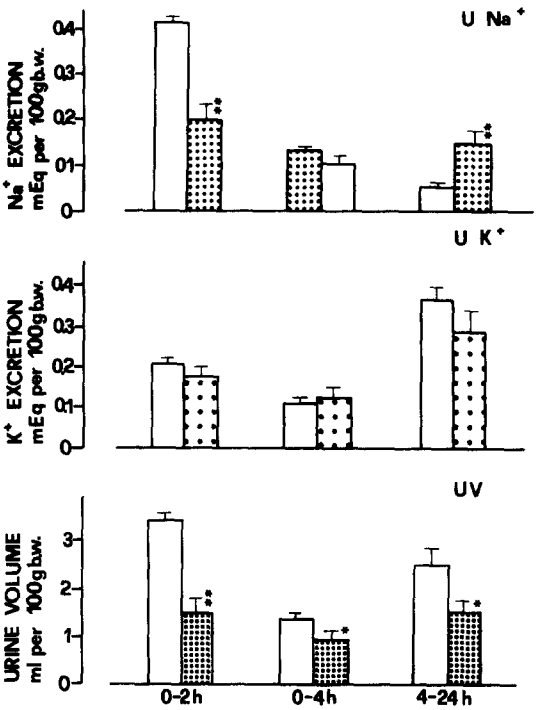

FIG. 6. Urine excretion following furosemide administration in controls (open bars) and in capsaicin-treated rats (dotted bars). Values are means ± S.E.M. of 11 capsaicin-treated subjects and of 12 controls. Difference from controls: $*p<0.05$; $**p<0.01$; where not indicated, difference from controls was not statistically significant.

that Na^+ excretion of capsaicin-treated rats was clearly different from that of controls. The overall analysis of variance revealed a nonsignificant neonatal treatment effect, $F(1,21)=3.660$, $p>0.05$, but a powerful neonatal treatment-time interaction, $F(2,42)=30.611$, $p<0.0001$. Planned pairwise comparison showed that Na^+ excretion of capsaicin-treated rats was markedly lower than that of controls during the first 2 h following furosemide injection; it was not statistically different during the second 2-h observation period, while it was significantly higher than that of controls in the remaining 20 hr of observation.

As shown in Table 1, the cumulative 24-h Na^+ excretion of capsaicin-treated rats was significantly lower than that of controls.

On the other hand, K^+ excretion of the 2 groups of rats was very similar at the different times of observation (Fig. 6). The analysis of variance revealed the absence of neonatal treatment

TABLE 1

CUMULATIVE URINE Na^+, K^+ AND VOLUME EXCRETION OF CONTROLS (CO) AND OF CAPSAICIN-TREATED RATS (CAPS) IN 24 h FOLLOWING FUROSEMIDE ADMINISTRATION

	Na^+ mEq/100 g b.wt.	K^+ mEq/100 g b.wt.	Volume ml/100 g b.wt.
CO	0.59 ± 0.02	0.63 ± 0.04	7.28 ± 0.46
CAPS	0.39 ± 0.05*	0.55 ± 0.10	4.09 ± 0.63†

Values are means ± S.E.M. of 11 capsaicin-treated subjects and of 12 controls. Difference from controls: $*p<0.05$; $†p<0.01$; where not indicated, difference from controls was not statistically significant.

effect, $F(1,21)=0.860$, $p>0.05$, in the absence of neonatal treatment-time interaction.

The cumulative 24-h K^+ excretion of capsaicin-treated rats was statistically indistinguishable from that of controls (Table 1).

Clear-cut differences were also detected for urine volume of capsaicin-treated and of control rats. The analysis of variance revealed a marked neonatal treatment effect, $F(1,21)=17.048$, $p<0.001$, together with neonatal treatment-time interaction, $F(2,42)=5.776$, $p<0.01$. The cumulative 24-h urine volume excretion of capsaicin-treated rats was significantly lower than that of controls (Table 1).

DISCUSSION

The results of the present experiments clearly demonstrate that neonatal capsaicin treatment only marginally affects salt intake control in the adult rat.

First of all, salt intake of capsaicin-treated rats in response to DOC was strictly similar and statistically indistinguishable from that of controls.

Again, no significant effect of capsaicin pretreatment was detected on salt appetite evoked by central renin injection, which acts through generation of angiotensin II (1). This hormone employs different brain mechanisms from those for mineralocorticoid-induced salt appetite (5).

Epstein and co-workers (6, 7, 27) showed that salt appetite following sodium depletion is elicited by the synergistic action of angiotensin II and of aldosterone, and pharmacological blockade of the receptors for both hormones completely suppresses the appetite. In this relation, it was puzzling to observe that capsaicin-treated rats had a lower salt intake than controls in response to sodium depletion, although being as sensitive as controls to the natriorexic actions of both renin and DOC.

However, the analysis of urine excretion to furosemide treatment showed that these differences in salt intake might be accounted for by a lower natriuretic response to furosemide in capsaicin-treated rats. In fact, capsaicin-treated rats showed lower Na^+ and urine volume excretion, while K^+ excretion was never significantly modified at the different times of observation.

Capsaicin treatment is known to alter the sensory and motor control of the bladder function (13,15), so that urine excretion occurs in frequent episodes and also with drippings. In these conditions, an exact measurement of urine parameters might be difficult, owing to increased adherence of urine to the animal fur. However, the differences observed in the urine excretion of the 2 animal groups cannot be explained just on the basis of technical artifacts or simply by an impairment of bladder voiding. Against this interpretation is: a) the finding that K^+ excretion was not affected, while Na^+ excretion and urine volume were; and b) Na^+ excretion was clearly reduced in the first 4 h of observation in capsaicin-treated rats, but a rebound effect was observed in the following 20 h when Na^+ excretion was higher in capsaicin-treated rats than in controls. If the differences in the parameters determined were just secondary to experimental urine loss, changes in the different parameters should have had similar trends and time courses.

Finally, neonatal capsaicin pretreatment affected neither the salt preference in rats which had not experienced previous sodium depletions, nor the "need-free" salt intake of rats exposed to repeated sodium depletions.

In conclusion, the results of present experiments indicate that neonatal capsaicin pretreatment does not alter either salt preference or salt appetite in the adult rat in response to hormonal treatment, mineralocorticoids or renin. Moreover, the lower salt intake observed in capsaicin-treated rats in response to sodium depletion appears to be secondary to reduced Na^+ excretion to furosemide.

In relation to the above-mentioned study (18) describing an enhanced development of hypertension in DOC-treated rats following neonatal capsaicin pretreatment, our results strongly suggest that this finding cannot be explained in terms of modifications of salt appetite. Since the present study has shown that renal responses can be altered by capsaicin pretreatment, it will be interesting to evaluate more directly whether altered renal function could account for the enhanced development of hypertension in DOC/salt-treated rats.

In relation to capsaicin effect on renal function, it is interesting to note that a previous study by Holzer-Petsche and Lembeck (13) has reported that also the renal excretion of an intragastric water load is altered by neonatal capsaicin treatment. Moreover, a recent study by Geppetti et al. (10) has shown the existence of a dense network of capsaicin-sensitive calcitonin gene-related peptide-containing nerves in the rat kidney. This innervation is greater in the medulla than in the cortex, and nerve fibers were detected also in the vicinity of renal tubules.

Salt intake is known to be influenced by gustatory signals from the oral cavity, by signals from the liver, as well as from the intravascular compartment (2, 4, 5, 11, 12, 14, 30, 32). In this relation, the negative results of the present study apparently suggest that sensory neurons controlling salt appetite are not capsaicin sensitive.

ACKNOWLEDGEMENTS

The authors wish to thank Prof. D. Ganten of the German Institute for High Blood Pressure for the generous gift of renin. The skillful technical assistance of M. Cucculelli, A. Fiorelli and M. Fede is gratefully acknowledged. This work was supported by a grant from Ministero Universitá e Ricerca Scientifica e Tecnologica, Rome (Fondi 60%).

REFERENCES

1. Avrith, D. B.; Fitzsimons, J. T. Renin-induced sodium appetite: Effects on sodium balance and mediation by angiotensin in the rat. J. Physiol. (Lond.) 337:479–496; 1983.
2. Blake, W. D.; Lin, K. K. Hepatic portal vein infusion of glucose and sodium solutions on the control of saline drinking in the rat. J. Physiol. (Lond.) 274:129–139; 1978.
3. Buck, S. H.; Burks, T. F. The neuropharmacology of capsaicin-review of some recent observations. Pharmacol. Rev. 38:179–226; 1986.
4. Contreras, R. J.; Kasten, T. Peripheral gustatory mechanisms of salt intake in the rat. In: de Caro, G.; Epstein, A. N.; Massi, M., eds. The physiology of thirst and salt appetite. New York: Plenum Press; 1986:479–484.
5. Denton, D. A. The hunger for salt. New York: Springer Verlag; 1982.
6. Epstein, A. N. Mineralocorticoids and central angiotensin may act together to produce sodium appetite. Peptides 3:493–494; 1982.
7. Fluharty, S. J.; Epstein, A. N. Sodium appetite elicited by by intracerebroventricular infusion of angiotensin II in the rat. II. Synergistic interaction with systemic mineralocorticoids. Behav. Neurosci. 97:746–758; 1983.
8. Frankmann, S. P.; Dorsa, D. M.; Sakai, R. R.; Simpson, J. B. A single experience with hyperoncotic colloid dialysis persistently alters water and sodium intake. In: de Caro, G.; Epstein, A. N.; Massi, M., eds. The physiology of thirst and salt appetite. New York: Plenum Press; 1986:115–121.
9. Ganten, D.; Speck, G.; Meyer, D.; Loos, H. E.; Schelling, R.; Rettig, R.; Unger, T. Biochemical and functional aspects of brain renin. In: Gross, T.; Vagel, G., eds. Enzymatic release of vasoactive peptides. New York: Raven Press; 1980:31–48.

10. Geppetti, P.; Baldi, E.; Castellucci, A.; Del Bianco, E.; Santicioli, P.; Maggi, C. A.; Lippe, I. T.; Amann, R.; Skofitsch, G.; Theodorsson, E.; Manzini, S. Calcitonin gene-related peptide in the rat kidney: Occurrence, sensitivity to capsaicin and stimulation of adenylate cyclase. Neuroscience 30:503–513; 1989.
11. Grossman, S. P. Thirst and sodium appetite. Physiological basis. San Diego: Academic Press; 1990:177–179.
12. Hermann, G. E.; Kohlerman, J.; Rogers, R. C. Hepatic vagal and gustatory efferent interaction in the brainstem of the rat. J. Auton. Nerv. Syst. 9:477–495; 1983.
13. Holzer-Petsche, U.; Lembeck, F. Systemic capsaicin treatment impairs the micturition reflex in the rat. Br. J. Pharmacol. 83:935–941; 1984.
14. Kaufman, S. Control mechanisms of salt appetite. In: de Caro, G.; Epstein, A. N.; Massi, M., eds. The physiology of thirst and salt appetite. New York: Plenum Press; 1986:459–463.
15. Maggi, C. A.; Meli, A. The role of neuropeptides in the regulation of micturition reflex. J. Auton. Pharmacol. 6:133–162; 1986.
16. Maggi, C. A.; Meli, A. The sensory-efferent function of capsaicin-sensitive sensory neurons. Gen. Pharmacol. 19:1–43; 1988.
17. Maggi, C. A.; Santicioli, P.; Geppetti, P.; Giuliani, S.; Patacchini, R.; Frilli, S.; Grassi, J.; Meli, A. Involvement of a peripheral site of action in the early phase of neuropeptide depletion following capsaicin desensitization. Brain Res. 436:402–406; 1987.
18. Manzini, S.; Bacciarelli, C. Enhanced development of deoxycorticosterone-induced hypertension in neonatally capsaicin-pretreated rats. Regul. Pept. 22:119; 1988.
19. Massi, M.; Epstein, A. N. Suppression of salt intake in the rat by neurokinin A: Comparison with the effect of kassinin. Regul. Pept. 24:233–244; 1989.
20. Massi, M.; Gentili, L.; Perfumi, M.; de Caro, G.; Schulkin, J. Inhibition of salt appetite in the rat following injection of tachykinins into the medial amygdala. Brain Res. 513:1–7; 1990.
21. Massi, M.; Perfumi, M.; de Caro, G.; Epstein, A. N. Inhibitory effect of kassinin on salt intake induced by different natriorexigenic treatments in the rat. Brain Res. 440:232–242; 1988.
22. Massi, M.; Polidori, C.; Gentili, L.; Perfumi, M.; de Caro, G.; Maggi, C. A. The tachykinin NH_2-senktide, a neurokinin B receptor agonist, is a very potent inhibitor of salt appetite in the rat. Neurosci. Lett. 92:341–346; 1988.
23. Massi, M.; Polidori, C.; Perfumi, M.; Gentili, L.; de Caro, G. Tachykinin receptor subtypes involved in the central effects of tachykinins on water and salt intake. Brain Res. Bull. 26:155–160; 1991.
24. Oetting Deems, R.; Friedman, M. I. Sodium chloride preference is altered in a rat model of liver disease. Physiol. Behav. 43:521–525; 1988.
25. Russel, L. C.; Burchiel, K. J. Neurophysiological effects of capsaicin. Brain Res. Rev. 8:165–176; 1984.
26. Sakai, R. R.; Frankmann, S. P.; Fine, W. B.; Epstein, A. N. Prior episodes of sodium depletion increase the need-free sodium intake of the rat. Behav. Neurosci. 103:186–192; 1989.
27. Sakai, R. R.; Nicolaidis, S.; Epstein, A. N. Salt appetite is suppressed by interference with angiotensin II and aldosterone. Am. J. Physiol. 251:R762–R768; 1986.
28. Szolcsanyi, J. Capsaicin-sensitive chemoceptive neural system with dual sensory-efferent function. In: Chahl, L. A.; Szolcsanyi, J.; Lembeck, F., eds. Antidromic vasodilation and neurogenic inflammation. Budapest: Akademiai Kiado; 1984:26–52.
29. Szolcsanyi, J. Sensory receptors and the nociceptive effects of capsaicin. In: Hakanson, R.; Sundler, F., eds. Tachykinin antagonists. Amsterdam: Elsevier; 1985:45–56.
30. Tordoff, M. G.; Schulkin, J.; Friedman, M. E. Hepatic contribution to satiation of salt appetite in rats. Am. J. Physiol. 251:R1095–R1102; 1986.
31. Wolf, G. Refined salt appetite methodology for rats demonstrated by assessing sex differences. J. Comp. Physiol. Psychol. 36:1012–1021; 1982.
32. Wolf, G.; Schulkin, J.; Simson, P. E. Multiple factors in the satiation of salt appetite. Behav. Neurosci. 98:661–673; 1984.