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THE EFFECT OF DEOXYCORTICOSTERONE ON SALT AND SUCROSE TASTE PREFERENCE THRESHOLDS AND DRINKING BEHAVIOUR IN RATS

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In an experiment in man, de Wardener & Herxheimer (1957) reported a lowering of the salt taste threshold during a period of high water intake. Other observations made in the experiment suggested that sodium was transferred from bone and/or cells into the extracellular fluid, and it seemed possible that the lowering of the taste threshold might be related to a loss of sodium from cells, either in the taste receptors or in the brain. It was therefore of interest to examine in an animal the effect on taste thresholds of a procedure known to lower the intracellular sodium concentration in the brain. The chronic administration of deoxycorticosterone acetate (DOCA) to rats is such a procedure (D. M. Woodbury, unpublished observations). In the present experiment salt and sucrose taste preference thresholds have been determined in rats before and during treatment with DOCA.

METHODS

The subjects were twelve male albino rats, aged approximately 90 days at the beginning of the experiment (December 8, 1958). They were individually housed in a constant-temperature room (25–25·5° C) with 24 hr illumination. The food consisted of powdered Purina Rat Chow (0·5 % NaCl). From December 8 to January 4 each rat received 10 g of this food daily; from January 5 until the end of the experiment 13 g was given daily, because there had been some loss of weight. The food offered was always completely consumed. The amount of food was restricted in order to keep the daily intake constant.

The animals were allotted at random to two groups; in one group salt and in the other sucrose taste thresholds were determined. The standard two-tube procedure was used, one tube containing the test solution, the other distilled water. Each test concentration was offered for 48 hr, the position of the solution being varied so that it occupied each side of the cage for 24 hr. The test solutions were presented in descending order of concentration except for a preliminary ascending series (November 17–December 5) which served to introduce the animals to the experimental situation. Each rat had the same two drinking tubes throughout each test series. At each change of concentration the tubes were alternated, so that the tube that had contained the solution for the previous 48 hr was filled

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with water, and vice versa. The test solutions which were used are given in the legends to Figs. 1–2.

The taste preference threshold was taken to be the lowest concentration at which more test solution was drunk than water, provided that the difference exceeded $\frac{1}{8}$ of the total fluid intake for the 48 hr. This threshold is marked by an arrow in each of the curves in Figs. 1 and 2; below the threshold an animal drinks water and test solution in approximately equal amounts. In 10 out of 30 threshold determinations irregularities of intake introduced some difficulty, as in some examples in Fig. 2. Then intakes at two successive concentrations (i.e. during 4 days) were added, and if the intake of test solution exceeded in the 4-day period the intake of water it was assumed that the threshold had not yet been passed. An excess greater than $\frac{1}{8}$ of the total intake was arbitrarily regarded as significant.

In the first test series (December 11–January 6) taste thresholds were determined for all the rats. On January 7 three rats in each group of six received an implant of seven 15 mg DOCA pellets under the skin of the back, the pellets being deposited singly at different sites. A 'sham' operation was performed on the other three rats in each group. Five days later the second series of taste threshold determinations was begun. Finally, on February 18, DOCA pellets were implanted in the animals that had acted as controls in the second test series; their taste thresholds were then determined for a third time (February 22– March 15). Between test series water was presented in both tubes.

RESULTS

The results are given in Table 1. The salt preference threshold fell sharply in each of the DOCA-treated animals (Fig. 1); little change occurred after sham treatment in the controls. The sucrose preference thresholds were more variable than those for salt and showed no consistent change, either in the DOCA-treated animals (Fig. 2) or the sham-treated controls. In the second part of the experiment the six animals that were previously controls were given DOCA. As before, the salt preference threshold fell during DOCA treatment, while the sucrose preference thresholds behaved inconsistently.

In addition to the changes in preference threshold certain changes occurred in the total fluid intake (Figs. 1 and 2). Invariably the intake was highest when the most concentrated solution of a series was presented, and then declined as the concentration was lowered, until it reached a 'basal' level. This basal intake remained essentially unchanged when the sapid solution was withdrawn and replaced by water at the end of the test series. The strength of the preference for a test solution can be assessed by the type of drinking behaviour. Below the preference threshold similar amounts of test solution and water are taken. At and above the preference threshold an animal drinks more test solution than water, but the total fluid intake remains the same. Then at higher concentrations it begins to drink so much more of the test solution that the total fluid intake increases, indicating that the preference is stronger than before. On the average the total intake exceeded the basal values when sodium chloride at a concentration about 20 times the salt preference threshold was offered or a sucrose solution about 6 times threshold. These ratios were not affected by DOCA.

Individuals differed widely in basal intake. The total fluid intakes in the first test series, before DOCA treatment, were similar in the control and treatment groups. In the second test series both the sham-operated and the DOCA-treated rats tended to drink more than in the first series, but the basal intake of the treated animals was much higher than that of the controls.

TABLE 1. Taste preference thresholds

		Thresholds for NaCl (g/100 ml.)		
Test period	Rat no.	1 Before sham implantation	2 After sham implantation	3 After DOCA implantation
Control animals: effect of sham implantation, followed by DOCA implantation	7	0·005	0·009	0·003
	9	0·009	0·016	0·0016
	11	0·009	0·009	0·0005
Geometric mean		0·007	0·011	0·0013
		Before DOCA implantation	After DOCA implantation	
Treated animals: effect of DOCA implantation only	8	0·03	0·00005	
	10	0·009	0·003	
	12	0·05	0·0009	
Geometric mean		0·024	0·0005	

		Thresholds for sucrose (g/100 ml.)		
Test period	Rat no.	1 Before sham implantation	2 After sham implantation	3 After DOCA implantation
Control animals: effect of sham implantation, followed by DOCA implantation	1	0·25	0·4	0·6
	3	0·1	0·4	0·1
	5	0·6	0·025	0·15
Geometric mean		0·25	0·16	0·2
		Before DOCA implantation	After DOCA implantation	
Treated animals: effect of DOCA implantation only	2	0·04	0·15	
	4	0·15	0·04	
	6	0·15	0·015	
Geometric mean		0·10	0·04	

Other observations

The manner in which the solutions were presented to the animals was designed to eliminate interference from any preference that a rat might have for one of the two drinking positions or for one of the tubes. Eight of the rats developed more or less strong position preferences; in some animals gradual changes in position preference occurred. Tube preference was noted only occasionally and was slight.

The amount of DOCA absorbed by the six animals that received implants was estimated by removing most of the pellets at the end of the second test series and weighing them. The mean weight per pellet removed after 42 days was 7·5 mg (S.D. 1·0); the animals therefore absorbed DOCA at the mean rate of 1·2 mg/day. Since their mean weight during the period of DOCA treatment was 297 g, the average daily dose was 4·0 mg/kg.

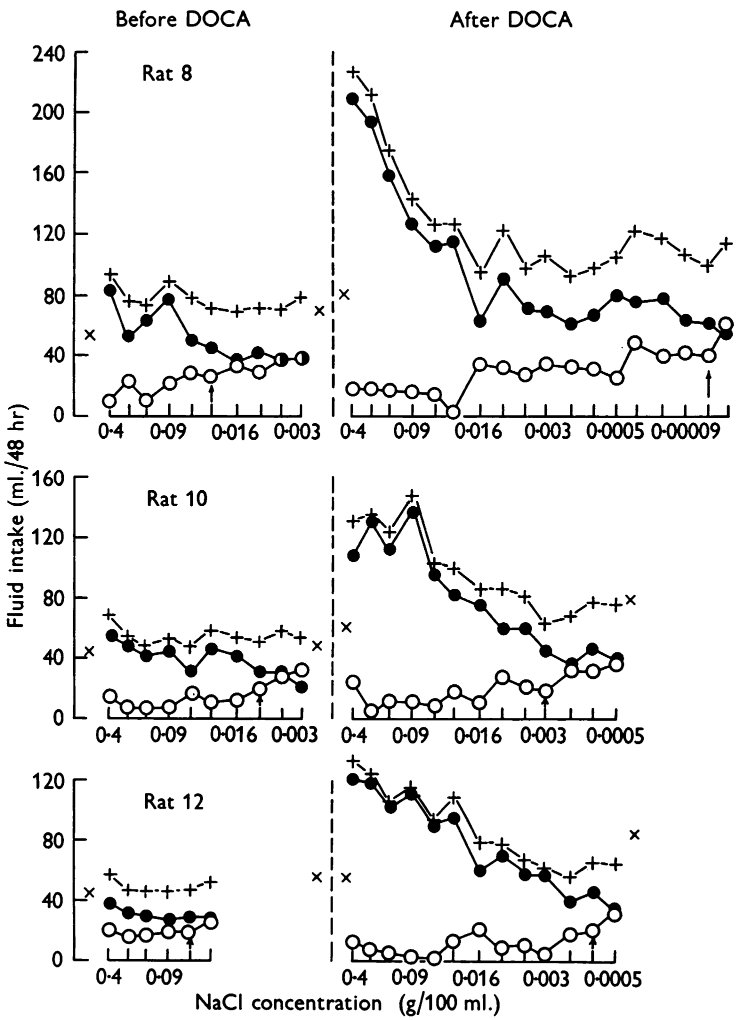

Fig. 1. Total fluid (+), salt solution (●) and distilled water (○) intakes of rats 8, 10 and 12 before and after implantation of DOCA pellets. Concentrations of sodium chloride (g/100 ml.) of 0·4, 0·25, 0·16, 0·09, 0·05, 0·03, 0·016, 0·009, 0·005, 0·003, 0·0016, 0·0009, 0·0005, 0·0003, 0·00016, 0·00009, 0·00005, 0·00003 were presented in successive periods of 48 hr; the second test series began 5 days after the implantation of DOCA. The lowest concentration of salt at which a rat drank more salt solution than water is the salt preference threshold(↑). The total intake for days on which water was presented in both drinking tubes is shown separately (×). Usually, two such days preceded and two followed each test series.

DISCUSSION

The changes in preference threshold following DOCA treatment were much greater and much more consistent for salt than for sucrose. It is unlikely that the changes in the sucrose threshold were related to the treatment. A lowered taste threshold for NaCl has also been observed in

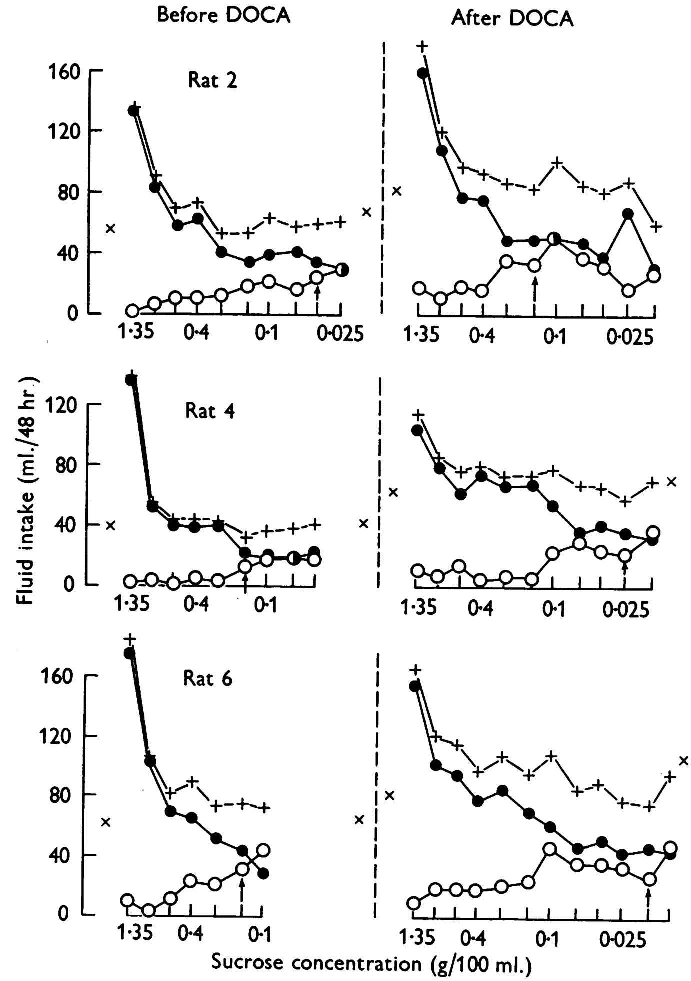

Fig. 2. Total fluid (+), sucrose solution (●) and distilled water (○) intakes of rats 2, 4 and 6 before and after DOCA implantation. Concentrations of sucrose (g/100 ml.) of 1·35, 0·9, 0·6, 0·4, 0·25, 0·15, 0·1, 0·06, 0·04, 0·025, 0·015, 0·01 were presented in successive periods of 48 hr; the second test series began 5 days after the implantation of DOCA. The sucrose preference threshold is indicated (↑). The total intake for days on which water was presented in both drinking tubes is shown separately (×). Usually two such days preceded and two followed each test series.

man during a period of high water intake (de Wardener & Herxheimer, 1957) and during sodium deprivation (Yensen, 1958*a*). It may be supposed that a decrease in the intracellular sodium concentration occurred in both these experiments. In a later experiment Yensen (1958*b*) studied the effect of water deprivation, which would be expected to cause a rise in intracellular Na concentration, and found that this led to a rise in the salt taste threshold.

The findings also agree with the observation that DOCA increases the appetite of rats for salt (Rice & Richter, 1943; Braun-Menéndez & Brandt, 1952). It is difficult, however, to relate the present results to Richter's (1939) and Bare's (1949) finding that the salt preference threshold is lowered by adrenalectomy. Both adrenalectomy and treatment with DOCA increase the salt appetite and lower the preference threshold, yet when adrenalectomized rats are given DOCA their salt consumption returns to normal (Richter, 1941). Adrenalectomy and DOCA treatment have opposite effects on the electrolyte distribution in the rat cerebral cortex, and on the electroshock seizure threshold (Woodbury, Timiras & Vernadakis, 1957). The observation that DOCA-treated rats become supersensitive to insulin and to anaphylaxis has led to the suggestion that DOCA may inhibit glucocorticoid secretion (Rosenberg, Woodbury & Sayers, 1952). If DOCA in fact leads to glucocorticoid deficiency, as does adrenalectomy, this might mediate the fall in salt preference threshold; the effect of cortisone on the threshold will have to be investigated. It will also be necessary to determine whether the effects of adrenalectomy and of DOCA treatment on the electrolyte distribution in other parts of the brain, particularly the hypothalamus, differ from those seen in the cortex (Stellar, 1954).

The results reported here do not help to locate the effect of DOCA on the salt preference threshold; it could be produced either at the sensory receptor, or centrally. However, the fact that adrenalectomy produces a similar effect may offer a clue to the site of action of DOCA, for it has been found that adrenalectomy affects neither the taste receptor threshold for salt (Pfaffmann & Bare, 1950) nor the psychophysical threshold, determined by a forced discrimination technique (Carr, 1952; Harriman & MacLeod, 1953). The first observation indicates that the lowering of the salt preference threshold after adrenalectomy is not due to a fall in receptor threshold; the second suggests that the central mechanism involved in psychophysical threshold determinations is separate from that mediating spontaneous taste preference behaviour. It may be that DOCA treatment, like adrenalectomy, affects only the latter mechanism.

Hitherto little attention has been paid to the phenomenon of extra fluid intake in taste preference experiments, although its existence is apparent in previous work (Richter, 1939; Bare, 1949; Young, 1949; Fregly, 1956). The extra fluid intake cannot be attributed to the need for increased water to excrete the extra solute load, because in the experiments with salt, where this argument might apply, the rats drank far more than the amount they required for this purpose. Moreover, the rats given sucrose, which is completely metabolized, showed a similar extra fluid intake. An indication that the taste of the solution may be responsible comes from the work of Sheffield & Roby (1950), who found that a solution of saccharine was an effective reward for learning in the rat. The present results give further support to the conclusion of Weiner & Stellar (1951) that 'the rat is so built that its rate of drinking is directly determined by the stimulus intensity of the...solution'. If one ventures to look beyond the austere and cautious wording, this may suggest that the rat drinks these solutions because it likes them, from greed rather than need.

SUMMARY

1. Salt and sucrose taste preference thresholds were determined in rats before and during treatment with DOCA.

2. A fall in the salt preference threshold occurred during DOCA treatment; no fall occurred in the control animals. The sucrose preference threshold did not change consistently in either group.

3. Attention is drawn to changes that occurred in total fluid intake during the preference-threshold determinations. At higher concentrations of salt or sucrose, considerably above the preference threshold, the total fluid intake was progressively greater than at concentrations near the preference threshold.

4. DOCA may exert its effect on the salt taste threshold by altering the intracellular electrolyte distribution in the brain, which it is known to do, or by affecting the taste receptors.

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