excluded, extrapolating from experiments on animals, that an alteration of the dopaminergic and enkephalinergic systems may be involved in this disorder, though the complexity of the numerous psychological factors involved should always be borne in mind. The precise way in which Nx enhances the sexual stimulant effect of NPA is as yet undetermined. We interpreted our findings as indicating that some Nx-actions are related to the dopaminergic mechanism, which would confirm the existence of a relationship between the action of opiates and dopamine-containing synapses in the brain[12,14-16]. One possible explanation of the influence of Nx on the NPA-effect would involve a Nx blockade of the opiate receptors that have an inhibitory effect upon the dopaminergic system involved in the control of sexual behavior.

On the other hand, the failure of Nx-pretreatment to potentiate the effect of a relatively high dose of NPA ($8\ \mu g \cdot kg^{-1}$) on mating behavior in sexually active rats may be because this NPA dose was already maximally active in these experiments. The findings in the present study on impotent rats would appear to contradict the observation by Gessa[2] that Nx induced a complete copulatory pattern in sexually inactive male rats. This discrepancy may well result from the different experimental conditions, however. In impotent rats, NPA ($8\ \mu g \cdot kg^{-1}$) was able to induce copulatory behavior in about 50% of the animals, confirming our previous results[10]. Nx-pretreatment did not alter the percentage of rats displaying the copulatory pattern, nor did it influence IF and EL, which were very low after NPA-treatment compared with the values for saline-treated sexually active rats. In conclusion, the ability of Nx to potentiate the NPA-effect on copulatory behavior can be observed only in a normally functioning physiological system, that is, in sexually active rats. In a situation of complete sexual inadequancy, that is in impotent males, while a strong dopaminergic agonist is still capable of activating sexual behavior in about 50% of rats, no stimulant effect of Nx can be shown.

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Mineralocorticoid treatment and the adrenalectomy-induced increase in monoamine oxidase activity[1]

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Summary. Bilateral adrenalectomy in the rat results in an increase in heart monoamine oxidase activity in animals drinking water and in animals drinking 0.9% saline. Daily administration of deoxycorticosterone acetate prevented the increased monoamine oxidase activity in the animals drinking saline but not in those drinking water.

As early as 1936, Richter[2] reported that normal rats drank similar amounts of sodium chloride solution and water when given a choice. In contrast, adrenalectomized animals were found to drink more of the saline solution. In another study, Richter[3] reported that administration of the synthetic mineralocorticoid, deoxycorticosterone acetate (DOCA), reduced sodium chloride intake to normal levels in adrenalectomized rats. Later, Fregly and Waters[4] schowed that administration of graded doses of either aldosterone or DOCA to adrenalectomized rats produced a 'U-shaped dose-reponse relationship' between percent change in intake of NaCl solution and dose of the drugs. That is, at low doses the sodium chloride intake was not decreased by the drugs and at high doses the appetite was actually increased while at intermediate doses the sodium chloride intake was decreased to control levels.

Bilateral adrenalectomy in the rat produces a number of changes other than alterations in sodium chloride appetite. Included among these are a decrease in blood pressure and increases in norepinephrine turnover, and monoamine oxidase (MAO) activity[5-10]. Each of these changes can be prevented by administration of appropriate doses of adrenal steroids.

In a previous study from this laboratory, it was shown that having the animals drink saline and administering daily doses of DOCA prevented the changes in blood pressure and in heart norepinephrine turnover and MAO activity[7]. In this same study the decrease in blood pressure was prevented by saline and low doses of glucocorticoids, either cortisol or corticosterone, but neither of these latter dosage schedules prevented the increase in heart norepinephrine turnover and MAO activity. Other authors have found that administration of larger doses of glucocorticoids among with saline to drink did prevent the adrenalectomy-induced increases in urinary catecholamine excretion and in tissue MAO activity[6,8,9]. Thus, many of the changes brought about by adrenalectomy can be prevented by administration of saline along with either a mineralocorticoid or a glucocorticoid provided that the steroid dosage is sufficient. The purpose of this work was to determine if the effects of DOCA on the adrenalectomy-induced increase in MAO activity are related to its effects on sodium metabolism.

Materials and methods. In these experiments, 200-250 g male Sprague-Dawley derived rats were adrenalectomized through a midline dorsal incision under pentobarbital anesthesia. Controls were sham-operated. All animals were

allowed free access to food. The 1st experiment was designed to determine the minimum dose of DOCA that would prevent the increase in MAO activity. In this 1st experiment, all adrenalectomized animals were given 0.9% saline as their only drinking fluid. Some of these adrenalectomized animals and all the control animals also received daily injections of 1 ml/kg of propylene glycol. The remaining adrenalectomized animals received either 300 or 500 µg/kg/day of DOCA dissolved in the propylene glycol vehicle. In a 2nd experiment, approximately half of the adrenalectomized animals were given 0.9% saline to drink and the remaining adrenalectomized animals received tap water and had rabbit salt spools placed in their cages. In this experiment, all animals received daily injections. Along with the controls, approximately half of the adrenalectomized animals received 1 ml/kg of propylene glycol. The remainder of the adrenalectomized animals received 500 µg/kg/day of DOCA dissolved in propylene glycol.

17 days after the surgery, heart MAO activity was determined according to a modification of the method previously described[10]. ^{3}H norepinephrine (6.25 nM) and ^{14}C phenethylamine (6.25 nM) were used as enzyme substrates. Animals were sacrificed by decapitation, their hearts were immediately removed and homogenized in cold 1.15% KCl. Analyses were carried out in duplicate with a 25-min incubation at 35 °C. Reactions were stopped through the addition of 2 N HCl, and after extraction with ethyl acetate an aliquot of the organic phase was taken for liquid scintillation counting. Incubation blanks were prepared by adding acid to the substrate prior to addition of the tissue homogenate. Preliminary experiments demonstrated that the reactions were linear for at least 40 min and that they were linear with respect to enzyme concentrations.

Statistical analyses for differences between means were carried out using a 2-tailed t-test.

Results and discussion. The effect of adrenalectomy on heart MAO activity in animals drinking 0.9% saline with norepinephrine as the enzyme substrate is shown in figure 1 and the effect with phenethylamine as the substrate is shown in figure 2. With each substrate, adrenalectomy caused a highly significant increase in enzyme activity. This increase was prevented by 500 µg/kg/day of DOCA but not by 300 µg/kg/day of the same drug. Thus, it appears that with saline as drinking fluid, 500 µg/kg/day of DOCA is

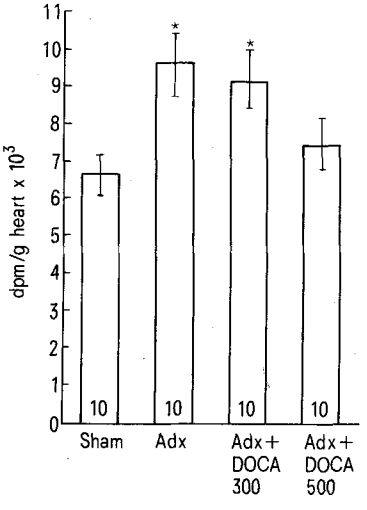

Figure 1. Heart MAO activity (mean ± SEM) with norepinephrine as substrate in sham-operated, adrenalectomized (Adx) and adrenalectomized DOCA-treated (Adx+DOCA) rats. 2 doses of DOCA (300 or 500 µg/kg/day) were employed. Numbers inside the histograms represent numbers of animals. *Different from sham $p < 0.02$.

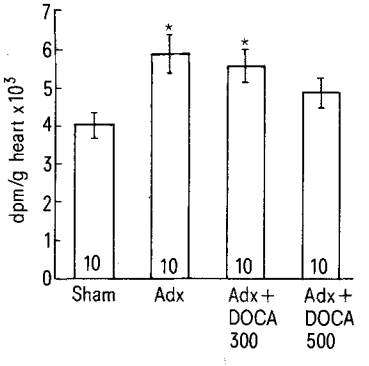

Figure 2. Heart MAO activity (mean ± SEM) with phenethylamine as substrate in sham-operated, adrenalectomized (Adx) and adrenalectomized DOCA-treated (Adx+DOCA) rats. 2 doses of DOCA (300 or 500 µg/kg/day) were employed. Numbers inside the histograms represent numbers of animals. *Different from sham $p < 0.01$.

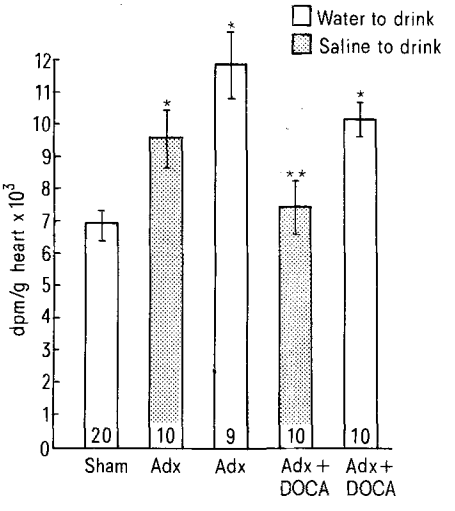

Figure 3. Heart MAO activity (mean ± SEM) with norepinephrine as substrate in sham-operated, adrenalectomized (Adx) and adrenalectomized DOCA-treated (Adx+DOCA) rats. Numbers inside the histograms represent numbers of animals. *Different from sham $p < 0.001$. **Not different from sham but different from each value marked by *$p < 0.025$.

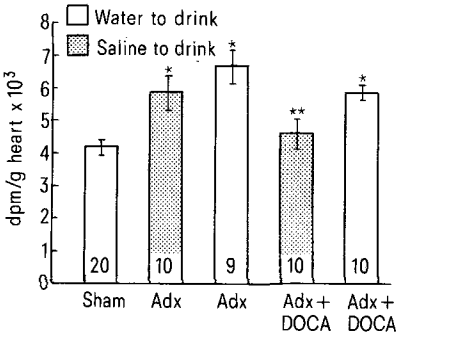

Figure 4. Heart MAO activity (mean ± SEM) with phenethylamine as substrate in sham-operated, adrenalectomized (Adx) and adrenalectomized DOCA-treated (Adx+DOCA) rats. Numbers inside the histograms represent numbers of animals. *Different from sham $p < 0.001$. **Not different from sham but different from each value marked by *$p < 0.025$.

very close to the minimum dose that prevents the statistically significant increase in MAO activity caused by adrenalectomy.

Because of its activity as a mineralcorticoid, DOCA causes retention of sodium. Giving the adrenalectomized animals an isotonic sodium chloride solution to drink also allows them to take in and utilize more sodium than if they had been drinking water. Thus, DOCA injections and saline to drink both help the adrenalectomized animals with their need for sodium. The combination of DOCA plus saline also prevents the adrenalectomy-induced increase in heart MAO activity. If DOCA prevents the adrenalectomy-induced increase in MAO activity because of its effects on sodium metabolism then decreasing the amount of sodium in the diet should decrease the capacity of DOCA to prevent the increased MAO activity. The 2nd experiment was designed to test this possibility. In this experiment, approximately half of the adrenalectomized animals were given 0.9% saline as their only drinking fluid and the remainder had water to drink and access to an alternate salt source. Approximately half of the animals in each of these groups received daily injections of DOCA. The results of this experiment are shown in figure 3 (norepinephrine as substrate) and figure 4 (phenethylamine as substrate). In the animals that had saline as their only drinking fluid, the enzyme activity increased to 139% of control (norepinephrine substrate) and 140% of control (phenethylamine substrate). In the animals drinking water, the enzyme activity increased to 171% of control with norepinephrine as the MAO substrate and to 160% of control with phenethylamine as the substrate (figs 3 and 4). Thus, the adrenalectomized animals drinking water appeared to have a greater increase in MAO activity than did the animals that had saline to drink. Additionally, daily administration of DOCA prevented the increase in MAO activity in the animals that had 0.9% saline to drink but did not cause a statistically significant suppression of the MAO activity in the animals drinking water. Thus, the dose of DOCA that was minimally effective at preventing the increase in MAO activity in animals drinking saline was ineffective at preventing the MAO activity increase when the animals were drinking water. Since this dose of DOCA suppressed the MAO increase in animals with a high sodium intake but not in animals with a lower sodium intake it is suggested that the action of DOCA on MAO activity may be related to its actions on sodium metabolism.

Other authors have found that daily glucocorticoid administration coupled with saline as the drinking solution prevents the adrenalectomy-induced increases in MAO activity[6,11,12]. The prevention of the increased enzyme activity has been attributed to an effect of the glucocorticoid. The results of the present study suggest that there may be a relationship between sodium intake and the adrenalectomy-induced change in MAO activity. Also, administration of an adrenal steroid, either a mineralocorticoid or a glucocorticoid appears to be necessary to completely prevent the change in the activity of this enzyme. At this time it is unclear whether mineralocorticoids and glucocorticoids suppress the adrenalectomy-induced increase in MAO activity through the same mechanism.

In summary, it can be said that the findings of this study show that mineralocorticoids and sodium together, but not alone prevented the adrenalectomy-induced increases in MAO activity.

1 Acknowledgment. This work was supported in part by a grant from the American Heart Association - Louisiana, Inc.
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Amantadine modulates phencyclidine binding site sensitivity in rat brain

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Summary. Amantadine, an antiviral drug with various CNS effects, significantly increases the affinity of the [^{3}H] PCP receptor in rat brain. Rimantadine, an analogue of amantadine devoided of CNS effects, does not have any affect on the [^{3}H] PCP receptor. These results may suggest that some of the CNS actions of amantadine are related to an interaction with the PCP receptor.

Amantadine (1-adamantanamine) is an antiviral drug which has been shown, unexpectedly, to improve the symptomatic condition of parkinsonian patients[2,3]. The mechanism of action related to this antiparkinsonism activity is not completely understood, but appears to be due to the dopamine-releasing properties of amantadine[4-6]. Compared to levodopa, amantadine is relatively free of side effects[7]. Interestingly, amantadine may cause severe mental symptoms in patients with a history of psychiatric disorders[7]. Since we have recently shown the existence of [^{3}H] phencyclidine (PCP) receptors in rat brain[8] and because PCP possesses a peculiar profile of psychotomimetic effects[9], we have decided to investigate the possible interaction of amantadine with the PCP binding site.

Materials and methods. Rat olfactory bulb slices were prepared as described before[8]. Frozen slide-mounted sections were preincubated for 15 min in 5.0 mM Tris-HCl, 50 mM sucrose, 20 mM NaCl, pH 7.4 at 0 °C followed by a 45-min incubation in the same buffer (without NaCl), pH 7.4 at 0 °C with various concentrations of [^{3}H] PCP (48 Ci/mmole; New England Nuclear) in the presence of various concentrations of amantadine or its inactive analogue, rimantadine. At the end of the incubation, the slides were transferred sequentially through 6 rinses (30 sec in