Effect of phencyclidine on fluid intake and urine excretion

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Phencyclidine hydrochloride, 1(1-phenylcyclohexyl) piperidine, also known as Sernyl or PCP, is an anaesthetic drug (Greifenstein, de Vault & others, 1958; Chen, Ensor & others, 1959), lately used only as an animal tranquillizer because of its severe central nervous side effects in man. Recently, it has gained increasing popularity among drug users as a hallucinogenic agent (Linden, Lovejoy & Costello, 1974), and hydration has been suggested as a therapeutic tool to assure adequate urinary output for secretion of the drug. Chen, Ensor & Bohner (1965) have shown that phencyclidine promotes the excretion of urine, and, therefore, I have examined the interdependence of fluid intake and urine output in the diuresis produced by the drug.

Phencyclidine hydrochloride was dissolved in saline and a dose of either 5 or 10 mg kg^{-1} was injected (s.c.) to a group of 5 male rats weighing about 200 g each. 0·9 % (w/v) saline was used for control injections. Before the administration of drug or saline, the animals were deprived of food for 16 h and of water for 2 h and their urinary bladders emptied. For 24 h after injection, the rats were kept in individual metabolic cages, and the volumes of both urine excretion and fluid intake were recorded. In each urine sample pH as well as sodium and potassium content were determined.

Three sets of experiments were carried out: I—with normally hydrated rats (the animals had free access to water or saline), II—with rats deprived of water; III—with animals given 10 ml of water by stomach tube just before injection.

During the first 6 h after drug administration, all the treated rats produced a significantly greater amount of urine than the respective control animals (Fig. 1), the output rate being maximal within the first 2 h. Only in set II was a pronounced dose-response effect retained for up to 24 h. In set I, the dose-response effect was slight at all times, and in spite of the increased diuresis observed during the initial period, the total urine volume excreted by the treated animals at the end of 24 h did not differ significantly from that of the controls. Both control and drug-treated animals consumed about the same amount of tap water (Fig. 2).

The temporary diuresis induced by phencyclidine was reflected 2–5 h after drug administration by an increase in the pH of the urine (6·4 in the controls, 7·6 in all treated groups). As expected, the higher pH was due to the presence of phencyclidine and its metabolites in the excreted urine (unpublished results).

A 5-fold increase in the sodium excretion by animals with free access to water was observed during diuresis up to 6 h after drug injection (Table 1). This increase

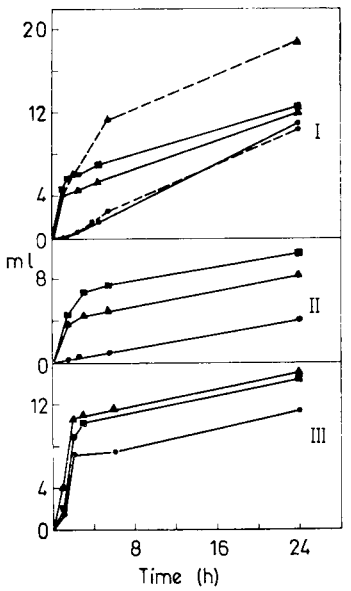

FIG. 1. Effect of phencyclidine on urine excretion. I. Rats with free access to water (—) or saline (– – –). II. Water-deprived rats. III. Water loaded rats. Amount of drug administered per rat: ●—none (control); ▲—5 mg kg^{-1}; ■ —10 mg kg^{-1}. Each experimental point represents an average value obtained from 5 rats. y axis—Cumulative urine excretion per rat (ml).

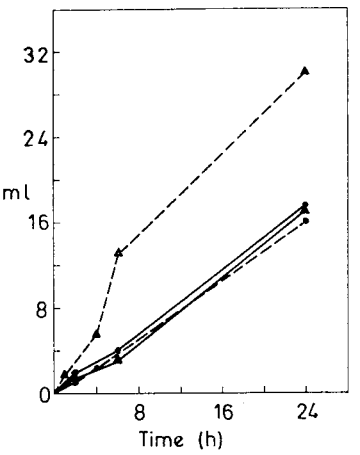

FIG. 2. Effect of phencyclidine on water and saline intake. (—) rats kept on water; (– – –) rats kept on saline. Amount of drug administered per rat: ●—none (control); ▲—5 mg kg^{-1}. Each experimental point represents an average value obtained from 5 rats. y axis —Cumulative fluid intake per rat (ml).

Table 1. *Effect of phencyclidine on urine output, fluid intake and electrolyte excretion of rats with free access to water or saline.*

	Water				Saline			
	Control		Phencyclidine		Control		Phencyclidine	
Parameter	0–6 h	6–24 h	0–6 h	6–24 h	0–6 h	6–24 h	0–6 h	6–24 h
Urine output (ml)	2·2 ± 0·2	9·5 ± 0·6	7 ± 0·4*	5·5 ± 0·4	2·5 ± 0·3	8 ± 0·5	11·5 ± 0·9*	7·3 ± 0·6
Fluid intake (ml)	3 ± 0·3	14·5 ± 1·5	3·8 ± 0·4	13 ± 1·2	3·8 ± 0·5	12 ± 1·3	13 ± 1·3*	17 ± 1·5
Sodium consumption (m equiv)	—	—	—	—	0·57 ± 0·07	1·8 ± 0·2	1·95 ± 0·2	2·6 ± 0·2
Sodium excretion (m equiv)	0·3 ± 0·04	1·4 ± 0·2	1·45 ± 0·2*	0·8 ± 0·04	0·34 ± 0·02	2 ± 0·2	2·55 ± 0·2*	1·8 ± 0·2
Sodium concentration in urine (m equiv ml^{-1})	0·14	0·15	0·2	0·14	0·14	0·25	0·22	0·25

Phencyclidine dose—5 mg kg^{-1}. The results are mean ± s.e.m. of 8 experiments. *$P < 0.05$ *vs* control

was not only due to the augmented urine flow of the treated animals (about 3 fold), but also to an enhanced sodium concentration (about 1·5 fold) in their urine. A concomitant rise in potassium excretion was also observed in the urine of the treated rats, but the rise was directly proportional to the increased urine flow, without change in concentration. Serum sodium concentration remained unchanged.

Because of the increase in sodium excretion, the animals of set I were given free access to saline instead of water. The fluid consumption of the controls kept on saline was close to that of the drug-injected rats kept on water, while the fluid consumption of the drug-injected animals kept on saline was much higher than that of the corresponding animals kept on water (Fig. 2). The increased saline intake of the treated rats was reflected by an elevated urine excretion (Fig. 1 and Table 1).

During the first 6 h, the average value of the ratio urine output/fluid intake was 0·65 ± 0·1 in the control rats kept on water and 0·6 ± 0·09 in those kept on saline. The corresponding value in the phencyclidine-treated animals kept on water was 1·75 ± 0·2, indicating pronounced dehydration in these rats. However, in the treated animals kept on saline, a ratio of 0·95 ± 0·06 was obtained, which is markedly lower than that of the corresponding animals kept on water, indicating that dehydration was significantly reduced by saline administration.

Between the sodium concentration of the treated rats kept on water and those kept on saline almost no difference was observed during the first 6 h (Table 1), in spite of the much larger sodium consumption of the animals in the latter group. After 6 h—which is comparable to the duration of the drug's pharmacological and metabolical actions (Domino, 1964; Millo & Chari-Bitron, 1975), the sodium concentration in the urine of all the treated animals reached the normal values of the corresponding control animals (Table 1).

The poor condition of the treated animals, resulting from dehydration and loss of sodium, could be partially prevented by giving the rats saline instead of water.

The author wishes to thank Prof. A. Kalir for supplying the phencyclidine and Miss Levana Motola for her skillful technical assistance.

August 9, 1976

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