Pharmacology Biochemistry & Behavior, Vol. 9, pp. 115–122. Printed in the U.S.A.

Short- and Long-Term Effects of Para-Chloroamphetamine on Ingestive Behavior[1]

J. M. STEIN,[2] M. J. WAYNER,[3] K. M. KANTAK AND R. C. COOK

Brain Research Laboratory, Syracuse University, Syracuse, NY 13210

(Received 17 April 1978)

STEIN, J. M., M. J. WAYNER, K. M. KANTAK AND R. C. COOK. *Short- and long-term effects of para-chloroamphetamine on ingestive behavior.* PHARMAC. BIOCHEM. BEHAV. 9(1) 115–122, 1978.—Para-chloroamphetamine (PCA) produces short-term decreases in eating and drinking. PCA also chronically decreases brain serotonin concentration following a single peripheral injection. The present investigation assessed short- and long-term effects of PCA on ingestive behavior and body weight in greater detail. Following an adaptation period, PCA, 0.0, 1.0, 2.0, 5.0 and 10.0 mg/kg, were administered IP, to free feeding rats. A decrease in food and water consumption was observed during the 0–24 hr postinjection period. During the 24–48 hr period, water consumption was significantly increased compared to baseline. Food intakes during this same period returned to baseline levels. No long-term effects on ingestive behavior or body weight were seen during the following 30 days.

Para-chloroamphetamine Body weight Anorectics Brain 5-HT Ingestive behavior Eating Drinking Serotonin

THERE is a considerable amount of evidence that para-chloroamphetamine (PCA) and para-chloromethamphetamine (PCMA) produce acute decreases in food consumption [6, 9, 18, 20]. These effects have been determined by measuring the amount of food consumed by food rationed rats or mice. With respect to these short-term effects on ingestive behavior, PCA is similar to amphetamine and several other phenylethylamines [2, 9, 14, 18, 20]. Unlike amphetamine, however, PCA and PCMA produce long-term changes in brain chemistry including decreases in concentrations of tryptophan hydroxylase, serotonin (5-HT), and 5-hydroxyindoleacetic acid [10, 13, 22, 24]. The possible long-term behavioral effects of PCA, therefore, might be similar to the effects observed following lesions of the raphe nuclei or following administration of several chemicals reported to lower brain 5-HT concentrations. Several hypotheses can be suggested concerning the long-term effects of PCA on eating and drinking. PCA might produce long-term hyperphagia and increased body weight. These effects would be similar to those observed following intraventricular, 5,7-dihydroxytryptamine (DHT) or p-chlorophenylalanine (PCPA; [3,23]). PCA might have no long-term effects on ingestive behavior. This would be in agreement with studies showing no long-term changes following electrolytic lesions of the median and dorsal raphe nuclei [4, 11, 17]. PCA might produce long-term hypophagia and hypodipsia. There is little support for this hypothesis among other studies. Finally, PCA might produce subtle changes in eating and drinking patterns. For example, intraventricular 5,6-DHT was shown to produce long-term changes in meal size and frequency of selected foods without affecting 24 hr total food intake [8].

While the long-term neurochemical effects of PCA have been studied, possible long-term changes in ingestive behavior have received little attention. A lack of long-term effects on eating and drinking [10,19] have been reported. These experiments, however, were primarily concerned with several other effects of the drug and the changes in ingestive behavior were not emphasized. A more thorough examination of effects of PCA on eating and drinking seemed necessary. The need for a more thorough study is also indicated by the large number of experiments on the long-term effects of PCA on other behaviors [7, 16, 21, 27, 33]. In addition, free feeding rats were used in the present experiment.

Since PCA, 5.9 or 10.0 mg/kg, produced short-term but no long-term effects on the intake of ethanol or saccharin solutions or water [29], the purpose of the present investigation was to examine the short- and long-term effects of PCA on ingestive behavior and body weight in greater detail. Following an adaptation period, individually housed free feeding rats were administered 0.0, 1.0, 2.0, 5.0 and 10.0 mg/kg of PCA. Food and water intakes and body weights were measured once per day for the next 30 days. Results indicate short-

[1]Supported by NSF Grant No. BNS 76-18520.

[2]Present address: Regional Primate Research Center, University of Washington, Seattle, WA 98195.

[3]Send reprint requests to M. J. Wayner at Brain Research Laboratory, Syracuse University, Syracuse, NY 13210.

term, 0–24 hr postadministration, hypophagia, hypodipsia, and body weight loss. Water consumption, food intakes, and body weights recovered following these initial deficits. No long-term effects on food and water consumption and body weights were observed during the next 30 days.

METHOD

Animals

Thirty-five female hooded rats, at least 4 months old and 220–323 g in weight, were selected from our colony and placed into individual cages, 25×28×30 cm. A 12 hr light-dark cycle began at 0700 hr and was followed by a 12 hr dark phase. The room temperature was maintained at 20±1°C.

Drugs

PCA injection solutions, 1.0, 2.0, 5.0 and 10.0 mg/cc calculated from the base, were prepared from d,l-para-chloroamphetamine hydrochloride (Sigma Chemical) dissolved in 0.9% NaCl in triple distilled water. Saline injections were of 0.9% NaCl. All injections were administered intraperitoneally in volumes of 1 cc/kg of body weight at 1800 hr.

Procedure

For a period of at least 10 days, Days 1–10, animals were adapted to their home cages. During this time and for the entire experiment, body weights and ad lib food and water intakes were measured daily between 1400 and 1600 hr. Data collected on Days 11–16 were used to determine the baseline measurements for each animal. On Days 17, 18 and 19 each animal received a saline injection. On Day 20, animals were divided into 5 groups of 7 rats each comprising the 0.0, 1.0, 2.0, 5.0 and 10.0 mg/kg groups. At 1800, animals in these groups were weighed and injected, respectively, with either 0.0 (saline), 1.0, 2.0, 5.0 or 10.0 mg/kg of PCA. On Days 21 and 22 all animals were injected with saline. Food and water intakes and body weights were recorded for the next 30 days.

RESULTS

Food and water intakes and body weights were analyzed by means of 5×12 analyses of variance. The factors were groups and days. The 5 levels of the group factor were the 0.0 (saline), 1.0, 2.0, 5.0 and 10.0 mg/kg groups. The 12 levels of the days factor were the mean intake of all animals during Days 11–16, the mean intake of all animals during Days 17–19, the 6 daily individual intakes on Days 20–25, and the mean intake of all animals during Days 26–32, Days 33–39, Days 40–46 and Days 47–53. The data for Days 20–25 were analyzed individually in order that the drug or saline injections on Day 20, the two final saline injections on Days 21 and 22, and the first three postinjection days on Days 23–25, could be examined in greater detail.

Analysis of food intakes indicated significant differences between groups, $F(4,30)=8.25$, $p<0.01$, and days $F(11,330)=63.04$, $p<0.01$. The groups by days interaction was also significant, $F(44,330)=6.57$, $p<0.01$. Simple main effects tests performed within each group revealed significant differences between days in the 1.0, 2.0, 5.0 and 10.0 mg/kg groups and no significant differences in the saline group. Figure 1 illustrates the mean food intakes of the 0.0, 5.0 and 10.0 mg/kg groups. Figure 2 illustrates the mean food intakes of the 0.0, 1.0 and 2.0 mg/kg groups. Within group analyses with Tukey A tests revealed significant decreases in food intakes on Day 20 when compared to the individual baseline period for the 1.0, 2.0, 5.0 and 10.0 mg/kg groups, $p<0.01$. There was a significant increase in food intakes on Day 22 compared to the baseline period in the 2.0 mg/kg

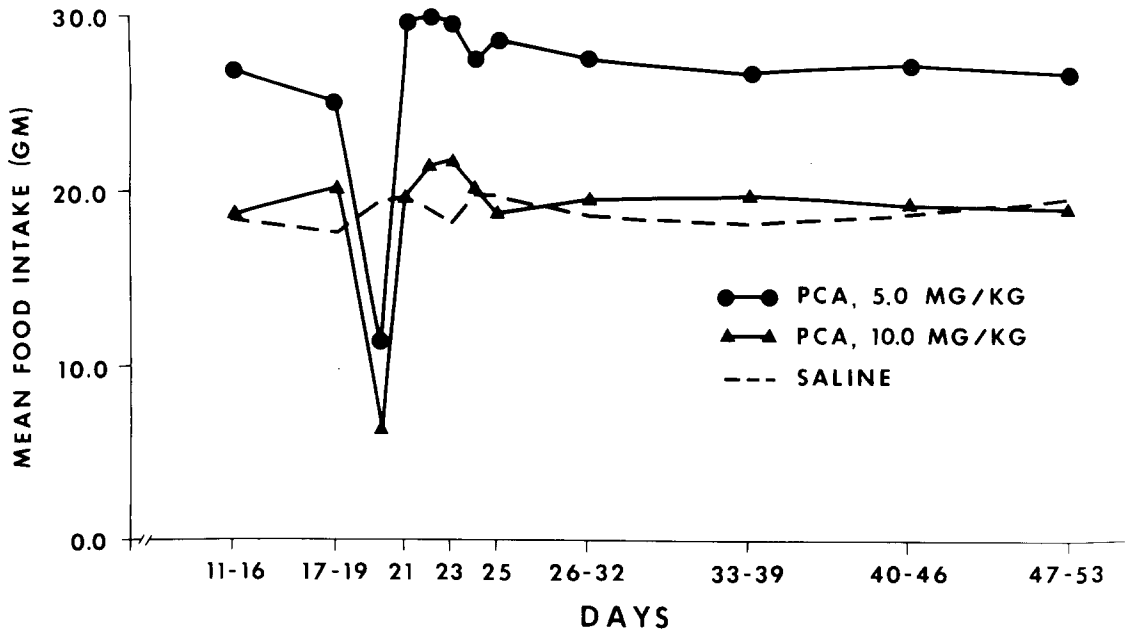

FIG. 1. Mean 24 food intake data in the saline, 5.0 and 10.0 mg/kg groups during the baseline period (Days 11–16), predrug saline injection days (Days 17–19), the drug day (Day 20), the two individual postdrug saline injection days (Days 21 and 22), and the next three individual postdrug days (Days 23, 24 and 25) and the mean of Days 26–32, 33–39, 40–46 and 47–53. n=7 animals/group.

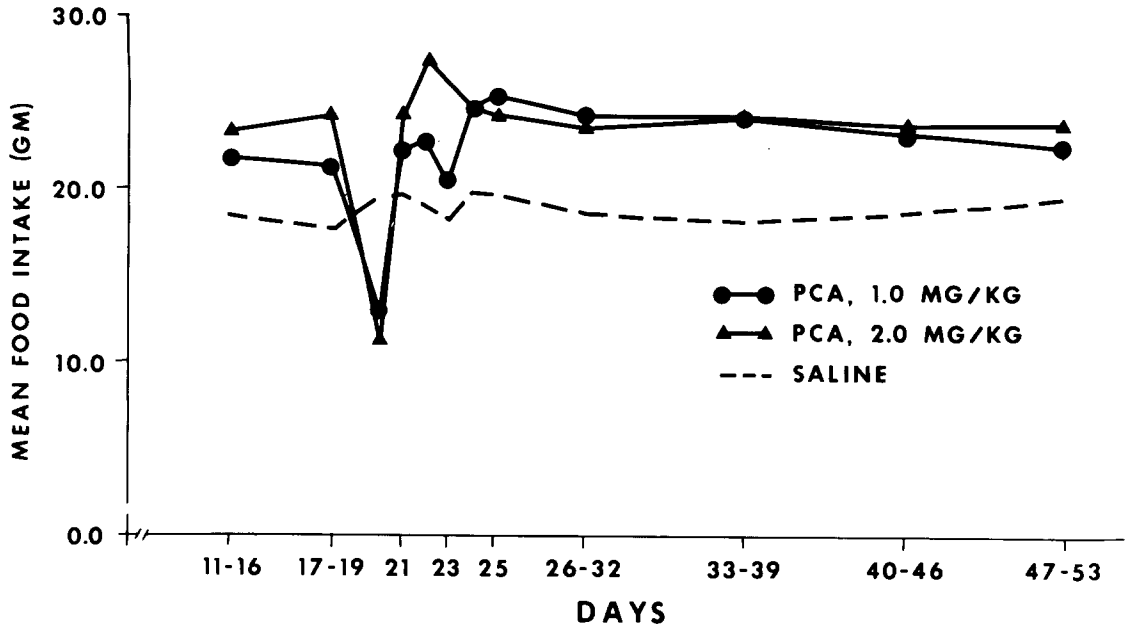

FIG. 2. Mean 24 hr food intake data in the saline, 1.0 and 2.0 mg/kg groups during the baseline period (Days 11–16), predrug saline injection days (Days 17–19), the drug day (Day 20), the two individual postdrug saline injection days (Days 21 and 22), the next three individual postdrug days (Days 23, 24 and 25) and the mean of Days 26–32, 33–39, 40–46 and 47–53. n=7 animals/group.

group, $p<0.05$. There were no significant differences within groups after Day 22. Between group Tukey A tests performed on food intakes among the 5 groups revealed significant differences during the baseline period. Further analyses comparing groups, therefore, were performed following conversion of food intakes to percentage change from each animal's baseline intake. This conversion and subsequent analysis was performed on data from Days 20 and 21 since the most notable drug effects occurred on these days. The percentage data were analyzed by means of a 5×2 analysis of variance. The factors were groups and days. The 5 levels of the groups factor were the 0.0, 1.0, 2.0, 5.0 and 10.0 mg/kg groups. The 2 levels of the days factor were Day 20, the 0–24 hr postinjection period, and Day 21, the 25–48 hr postinjection period.

Analysis of percentage change in food intake indicated significant differences among groups, $F(4,30)=7.91p<0.01$, and between days, $F(1,30)=122.57$, $p<0.01$. The groups by days interaction was also insignificant, $F(4,30)=6.24$, $p<0.01$. Figure 3 illustrates the mean percentage change in food intake for each group during the 0–24 hr and during the 25–48 hr postinjection periods. Further analysis with Tukey A tests revealed significant decreases in percentage food intake change on Day 20 in the 1.0, 2.0, 5.0 and 10.0 mg/kg groups compared to the 0.0 group, $p<0.01$. There were no significant differences in percentage intakes changes on Day 20 among the various PCA doses. On Day 21, there were no significant differences among the 0.0, 1.0, 2.0, 5.0 and 10.0 mg/kg groups.

In summary, PCA produced significant decreases in food intakes on Day 20 during the first 24 hr postinjection period. There were no significant differences during this period among the various PCA doses. Food intakes in the 1.0, 2.0, 5.0 and 10.0 mg/kg groups returned to baseline levels on Day 21. Intakes in the 2.0 mg/kg group exhibited a significant increase on Day 22.

Analaysis of water intakes indicated significant differences between groups, $F(4,30)=8.54$, $p<0.01$, and days, $F(11,330)=61.86$, $p<0.01$. The groups by days interaction was also significant, $F(44,330)=7.35$, $p<0.01$. Simple main effects tests performed within each group revealed significant differences among days in the 1.0, 2.0, 5.0 and 10.0 mg/kg groups and no significant differences in the saline group. Figure 4 illustrates the mean water intakes in the 0.0, 5.0, 10.0 mg/kg groups. Figure 5 illustrates the mean water intakes in the 0.0, 1.0, and 2.0 mg/kg groups. Within group analyses with Tukey A tests revealed significant decreases in water intakes on Day 20 when compared to the individual baseline period in the 1.0, 2.0, 5.0 and 10.0 mg/kg groups, $p<0.01$. There were significant increases in water intakes on Day 21 compared to the baseline period in the 2.0, 5.0 and 10.0 mg/kg groups, $p<0.01$. In the 5.0 group, water intakes remained elevated compared to the baseline period on Day 22, $p<0.01$, and Day 23, $p<0.05$. Between group Tukey A tests performed on water intakes among the 5 groups revealed significant differences during the baseline period. Further analyses comparing groups, therefore were performed following conversion of water intakes to percentage change from each animal's baseline intake. This conversion and subsequent analysis was performed on data from Days 20 and 21 since the most notable drug effects occurred on these days. The percentage intake data were analyzed by means of a 5×2 analysis of variance. The factors were groups and days. The 5 levels of the groups factor were 0.0 (saline), 1.0, 2.0, 5.0 and 10.0 mg/kg groups. The 2 levels of the Days factor were Day 20, the 0–24 hr postinjection period, and Day 21, the 25–48 hr postinjection period.

Analysis of percentage change in water intake indicated

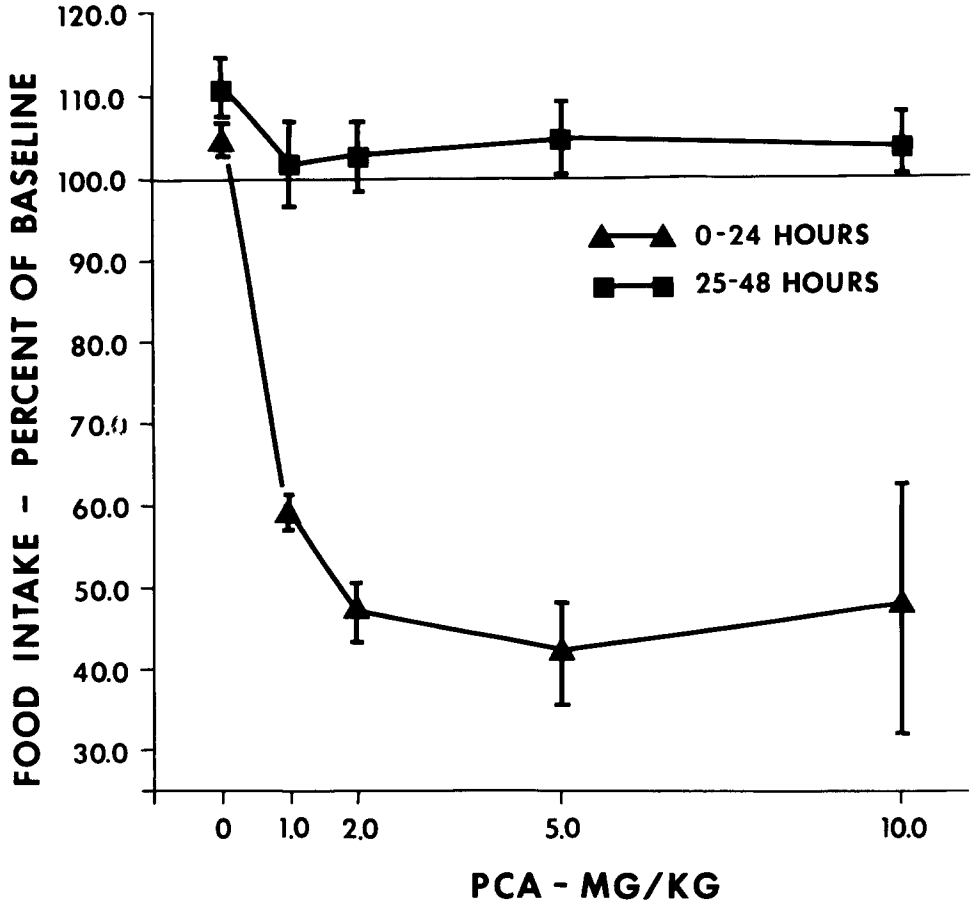

FIG. 3. Mean (±SEM) percentage food intakes following 0.0 (Saline), 1.0, 2.0, 5.0 and 10.0 mg/kg of PCA on the drug day (0–24 hr) and postdrug day (25–48 hr). Each point represents the mean of 7 animals based upon each animal's food intakes during the baseline period.

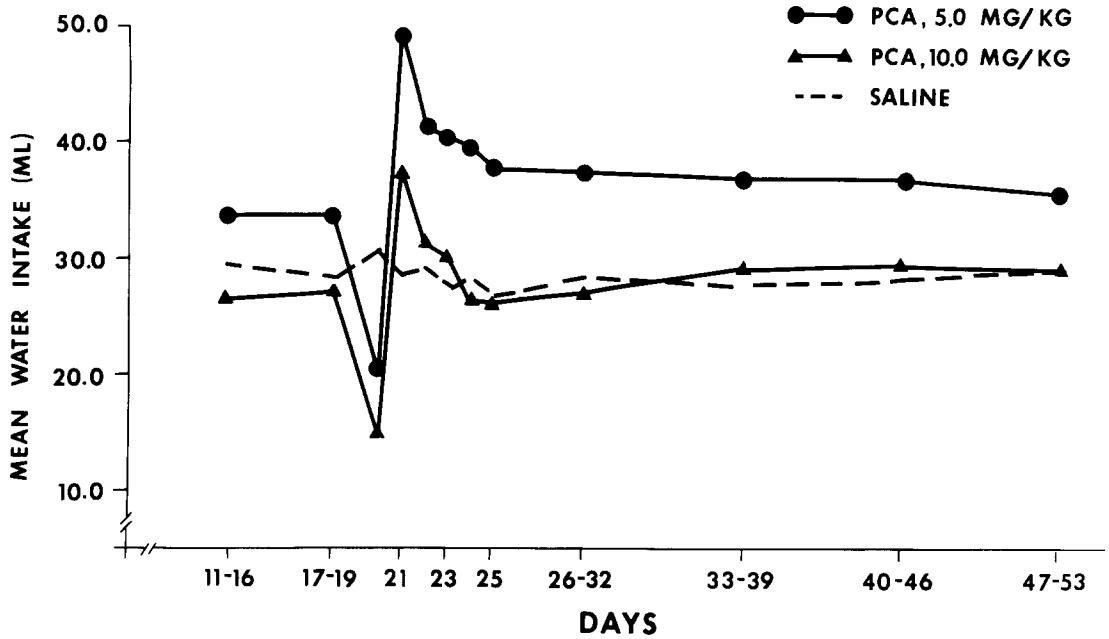

FIG. 4. Mean 24 hr water intake data in the saline, 5.0 and 10.0 mg/kg groups during the baseline period (Days 11–16), predrug saline injection days (Days 17–19), the drug day (Day 20), the two individual postdrug saline injection days (Days 21 and 22), the next three individual postdrug days (Days 23, 24 and 25) and the mean of Days 26–32, 33–39, 40–46 and 47–53. n=7 animals/group.

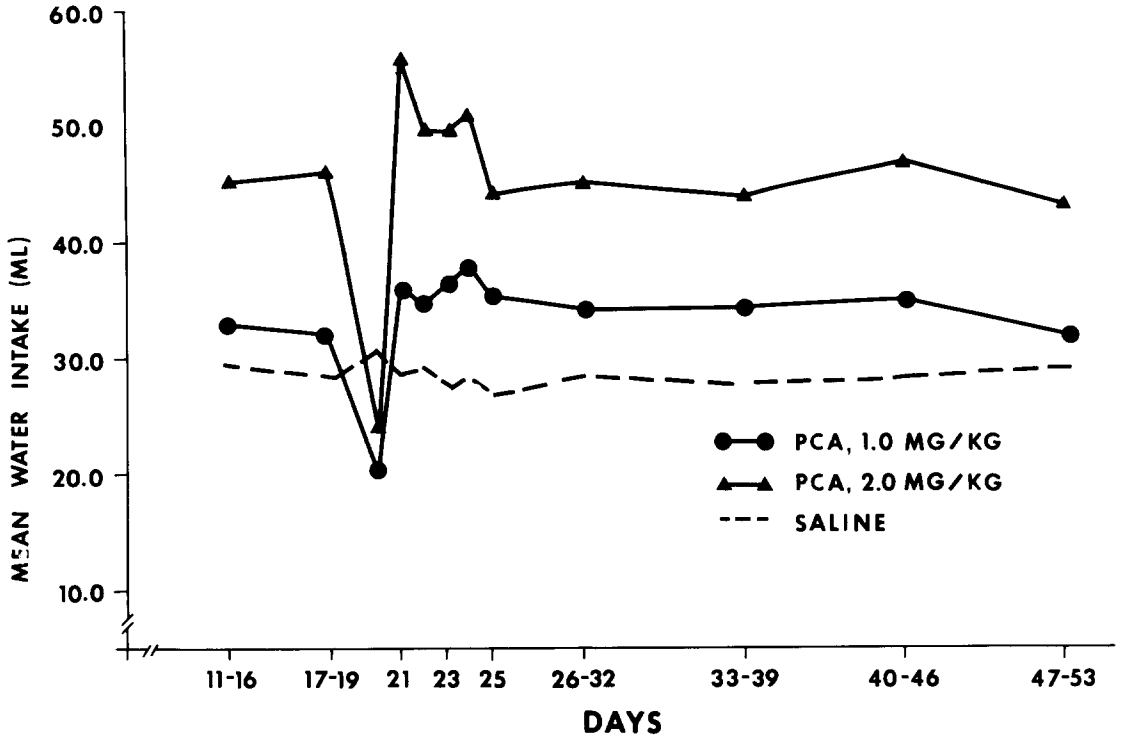

FIG. 5. Mean 24 hr water intake data in the saline, 1.0 and 2.0 mg/kg groups during the baseline period (Days 11–16), predrug saline injection days (Days 17–19), the drug day (Day 20), the two individual postdrug saline injection days (Day 21 and 22), the next three individual postdrug days (Days 23, 24 and 25) and the mean of Days 26–32, 33–39, 40–46 and 47–53. n=7 animals/group.

significant differences among groups, $F(4,30)=6.36, p<0.01$, and between days, $F(1,30)=267.00, p<0.01$. The groups by days interaction was also significant, $F(4,30)=24.39$, $p<0.01$. Figure 6 illustrates the mean percentage change in water intake for each group during the 0–24 hr and during the 25–48 hr postinjection periods. Further analyses with Tukey A tests revealed significant decreases on Day 20 in the 1.0, 2.0, 5.0 and 10.0 mg/kg groups compared to the 0.0 mg/kg group, $p<0.01$. There were no differences in percentage water intake change on Day 20 among the various PCA doses. On Day 21, there were significant increases in percentage water intake change in the 2.0 group compared to the 0.0 mg/kg group, $p<0.05$, and in the 5.0 and 10.0 groups compared to the 0.0 mg/kg group, $p<0.01$. In addition, there were significant differences in the 5.0 group compared to the 1.0 mg/kg group, $p<0.01$, and in the 10.0 group compared to the 1.0 mg/kg, $p<0.05$.

In summary, PCA produced significant decreases in water intakes on Day 20 during the first 24 hr postinjection period. There were no significant differences during this period among the various PCA doses. A significant increase in water intakes occurred during the 25–48 hr postinjection period in the 2.0, 5.0 and 10.0 mg/kg groups. These increases were dose dependent and the largest increase occurred at the

TABLE 1

BODY WEIGHT (G ± SEM) FOR EACH GROUP DURING VARIOUS DAYS OF THE EXPERIMENT

Group (PCA: mg/kg) n=7	Days 11-16 (Baseline Period)	Day 20 (0-24 hr postinjection period)	Day 53	Net Body Weight Change During the Entire Experiment (g ± SEM)
0.0	262.6 ± 9.1	265.4 ± 9.3	280.0 ± 9.5†	+17.4 ± 3.6
1.0	288.1 ± 12.2‡	279.1 ± 12.8†	307.1 ± 13.1†	+19.0 ± 4.5
2.0	297.1 ± 10.7‡	293.0 ± 12.5	316.6 ± 12.2†	+19.4 ± 2.5
5.0	283.1 ± 5.9‡	275.0 ± 7.8*	304.6 ± 6.0†	+21.4 ± 2.7
10.0	256.7 ± 8.6	252.0 ± 8.7	272.3 ± 10.3†	+15.6 ± 2.7

* Significantly different from the Baseline Period, $p<0.05$.
† Significantly different from the Baseline Period, $p<0.01$.
‡ Significantly different from the 0.0 Group, $p<0.01$.

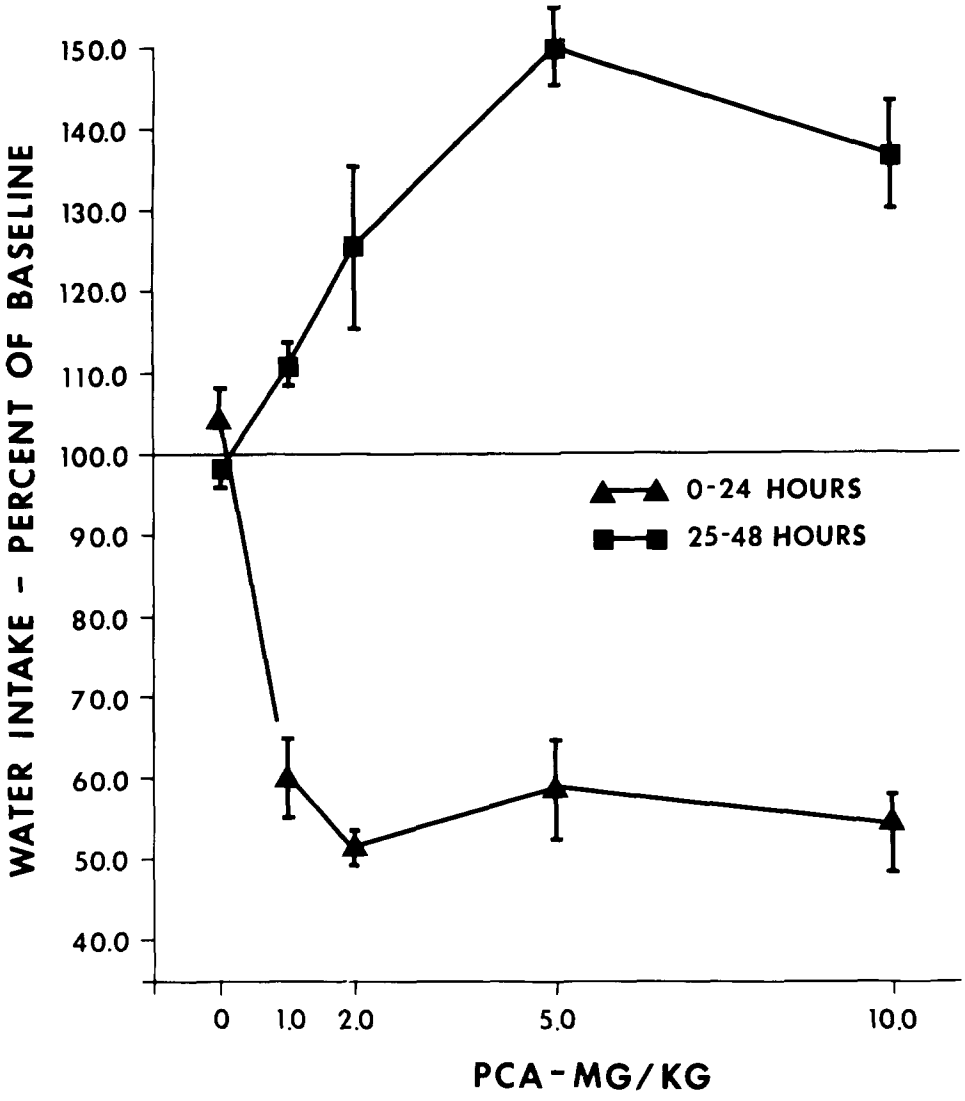

FIG. 6. Mean (±SEM) percentage water intakes following 0.0 (Saline), 1.0, 2.0, 5.0 and 10.0 mg/kg of PCA on the drug day (0–24 hr) and postdrug day (25–48 hr). Each point represents the mean of 7 animals based upon each animal's water intakes during the baseline period.

5.0 mg/kg dose. Intakes in the 5.0 mg/kg group remained elevated on Days 22 and 23. There were no significant differences in water intakes within any of the groups after Day 23.

Analysis of body weights indicated significant differences among groups, $F(4,30)=3.36$, $p<0.05$, and days, $F(11,330)=103.17$, $p<0.01$. The groups by days interaction was also significant, $F(44,330)=2.19$, $p<0.01$. Simple main effects tests performed within each group revealed significant differences among days in the saline and in the 1.0, 2.0, 5.0 and 10.0 mg/kg groups. Within group analyses with Tukey A tests revealed significant decreases in body weights on Day 20 compared to the individual baseline periods for the 1.0 group, $p<0.01$, and 5.0 group, $p<0.05$. Following Day 20, there were significant increases in body weights in all groups during the next 30 days. There were no significant differences in the rate of growth among the saline and PCA groups during this postdrug period. These data are listed in Table 1 which illustrates the body weight during the baseline period on Day 20, on Day 53, and the net body weight growth from the baseline period to Day 53. There were significant differences in body weight during the baseline period. Body weights in the 1.0, 2.0 and 5.0 mg/kg groups were significantly higher than the 0.0 or 10.0 mg/kg groups, $p<0.01$. Conversion of body weight during the experiment to percentages of baseline weights revealed no significant differences in body weight between groups.

In summary, PCA produced decreases in body weights on Day 20 during the first 24 hr postinjection period in the 1.0 and 5.0 mg/kg groups. Body weights in all groups returned to baseline levels on Day 21. There was no evidence that the drug changed the growth rate at any of the doses tested.

All PCA doses produced a behavioral syndrome reported previously for increased extraneuronal 5-HT [12,32] which includes body tremors, rigidity, reciprocal forepaw treading, hindlimb abduction, lateral head weaving, and piloerection. Observations made on Day 20 indicate that the syndrome

was displayed by all PCA injected rats within 5 min postinjection and endured for 3–6 hr.

DISCUSSION

These data demonstrate that PCA produces short-term changes in eating, drinking and body weight. During the 0–24 hr postinjection period significant decreases in food and water intakes occurred following 1.0, 2.0, 5.0 and 10.0 mg/kg of PCA. There were no significant differences in the magnitude of these decreases among the various PCA doses. Significant body weight decreases occurred during the 0–24 hr postinjection period following 1.0 and 5.0 mg/kg only. During the 24/48 hr postinjection period, PCA produced dose dependent increases in drinking. Food intakes and body weights returned to baseline levels. In contrast, long-term changes in ingestive behavior or body weight were not observed.

The physiological mechanisms by which PCA acutely decreases food and water intakes and body weight might be related to the central action of the drug on 5-HT, DA, or NE. PCA has been shown to increase the extraneuronal concentrations of these transmitters shortly after administration, thereby depleting the intraneuronal stores of these compounds [5, 25, 30, 31]. Within 24 hr the intraneuronal concentrations of the catecholamines are restored whereas 5-HT remains depleted because the tryptophan hydroxylase enzyme remains inhibited. If the decreases in eating and drinking are a result of a direct action of one or more of these neurotransmitters, it must be determined. It is important to note that the behavioral syndrome which is serotonergically mediated [12,32] and occurs shortly following PCA administration could have disrupted the animal's eating and drinking patterns. Therefore, the decreases in eating and drinking might be secondary to a motor disturbance produced by PCA. Also, PCA produces hyperthermia which endures for several hours and could thereby affect 24 hr intakes and body weight [18, 20, 26].

The dose dependent increase in drinking during the 24–48 hr postinjection period is interesting because it occurred without a concurrent increase in eating. These effects are difficult to explain but they might be related to a specific effect of PCA on water intake and fluid balance. Clearly, the increased water consumption is not prandial and food related. These effects are being investigated further.

There were no long-term effects of PCA on ad lib food and water intakes or body weight. Since there is a long-term depletion of 5-HT by PCA, a reduced level of 5-HT in the brain does not appear to influence these functions under these conditions. A supersensitivity in the serotonergic neurons might have developed. However, such a supersensitivity of serotonergic neurons following PCA remains to be demonstrated. Another explanation for the lack of long-term effects might be related to the route of drug administration. Peripherally administered PCPA does not affect long-term intakes and body weight [28] whereas intraventricularly administered 5,7-DHT and PCPA do have such effects [3,23]. Perhaps intraventricular PCA infusions would produce similar results provided that the underlying mechanism is serotonin related, since the three drugs have different biochemical actions [1, 10, 13, 15, 22, 24].

REFERENCES

1. Baumgarten, H., L. Lachemayer, A. Bjorklund, A. Nobin and E. Rosengren. Long-term recovery of serotonin concentrations in the rat CNS following 5,6-dihydroxytryptamine. *Life Sci.* **12:** 357–364, 1973.
2. Biel, J. H. Structure-activity relationships of amphetamine and derivatives. In: *International Symposium on Amphetamines and Related Compounds*, edited by E. Costa and S. Garrattini. New York: Raven Press, 1976, pp. 3–19.
3. Breisch, S. T., F. P. Zemlan and B. G. Hoebel. Hyperphagia and obesity following serotonin depletion by intraventricular p-chlorophenylalanine. *Science* **192:** 382–384, 1976.
4. Carey, R. J. Effects of selective forebrain depletions of norepinephrine and serotonin on the activity and food intake effects of amphetamine and fenfluramine. *Pharmac. Biochem. Behav.* **5:** 519–523, 1975.
5. Carr, L. A. and K. E. Moore. Release of norepinephrine and normetanephrine from cat brain by central nervous system stimulants. *Biochem. Pharmac.* **19:** 2671–2675, 1970.
6. Clineschmidt, B. F., J. C. McGuffin and A. B. Werner. Role of monoamines in the anorexigenic actions of fenfluramine, amphetamine and p-chloromethamphetamine. *Eur. J. Pharmac.* **27:** 313–323, 1974.
7. Davis, M. and M. H. Sheard. p-Chloroamphetamine: acute and chronic effects on habituation and sensitization of the acoustic startle response in rats. *Eur. J. Pharmac.* **35:** 261–266, 1976.
8. Diaz, J., G. Elison and D. Masuoka. Opposed behavioral syndromes in rats with partial or more complete central serotonergic lesions made with 5,6-dihydroxytryptamine. *Psychopharmacologia* **37:** 67–69, 1974.
9. Frey, H. H. p-Chloroamphetamine-similarities and dissimilarities to amphetamine. In: *International Symposium on Amphetamines and Related Compounds*, edited by E. Costa and S. Garanttini. New York: Raven Press, 1970, pp. 343–347.
10. Fuller, R. W. and H. D. Snoddy. Long-term effects of 4-chloroamphetamine on brain 5-hydroxyindole metabolism in rats. *Neuropharmacology* **13:** 85–90, 1974.
11. Fuxe, K., L. -O. Farnebo, B. Hamburger and S. -O. Ogren. On the in vivo and in vitro actions of fenfluramine and its derivatives on central monoamine neurons, especially 5-hydroxytryptamine, and their relation to the anorectic activity of fenfluramine. *Postgrad. Med. J.* **51:** Suppl. **1:** 34–45, 1975.
12. Grahame-Smith, D. G. Studies in vivo on the relationship between brain tryptophan, brain 5-HT synthesis and hyperactivity in rats treated with a monoamine oxidase inhibitor and L-tryptophan. *J. Neurochem.* **18:** 1053–1066, 1971.
13. Harvey, J. A., S. E. McMaster and L. M. Yunger. p-Chloroamphetamine: selective neurotoxic action in brain. *Science* **187:** 841–843, 1975.
14. Innes, I. R. and M. Nickerson. Norepinephrine, epinephrine and the sympathomimetic amines. In: *The Pharmacological Basis of Therapeutics*, 5th edition, edited by L. S. Goodman and A. Gilman. New York: MacMillan Publishing Co., 1975, pp. 477–513.
15. Koe, B. and A. Weissman. p-Chlorophenylalanine: a specific inhibitor of brain serotonin. *J. Pharmac. exp. Ther.* **154:** 499–516, 1966.
16. Lorens, S. Effects of chlordiazepoxide, d-amphetamine, morphine and zimelidine on lateral hypothalamic self-stimulation following 4-chloro-amphetamine. Presented at the Seventh Annual Meeting of the Society for Neuroscience, Anaheim, California, 1977.
17. Lorens, S. A., J. P. Sorenson and L. M. Yunger. Behavioral and neurochemical affects of lesions in the raphe system of the rat. *J. comp. physiol. Psychol.* **77:** 48–52, 1971.

18. Mantegazza, P., E. E. Muller, M. K. Naimzada and M. Riva. Studies on the lack of correlation between hyperthermia, hyperactivity and anorexia induced by amphetamine. In: *International Symposium on Amphetamines and Related Compounds*, edited by E. Costa and S. Garattini. New York: Raven Press, 1970, pp. 559–575.
19. Messing, R. B., L. Phebus, L. A. Fisher and L. D. Lytle. Effects of p-chloroamphetamine on locomotor activity and brain 5-hydroxyindoles. *Neuropharmacology* **15:** 157–163, 1976.
20. Nielsen, C. K., M. P. Magnussen, E. Kampmann and H. -H. Frey. Pharmacological properties of racemic and optically active p-chloroamphetamine. *Arch Int. Pharmacodyn Ther.* **170:** 428–443, 1967.
21. Ogren, S. O., C. Kohler, S. B. Ross and B. Srebro. 5-Hydroxytryptamine depletion and avoidance acquisition in the rat. Antagonism of the long term effects of p-chloroamphetamine with a selective inhibitor of 5-hydroxytryptamine uptake. *Neurosci. Letters* **3:** 341–347, 1976.
22. Pletscher, A., W. P. Burkhard, H. Bruderer and K. F. Gey. Decrease of cerebral 5-HT and 5-hydroxyindoleacetic acid by an aryl alkyl amine. *Life Sci.* **2:** 828–833, 1963.
23. Saller, C. F. and E. M. Stricker. Hyperphagia and increased growth in rats after intraventricular injection of 5,7-dihydroxytryptamine. *Science* **192:** 385–387, 1976.
24. Sanders-Bush, E., J. A. Bushing and F. Sulser. Long term effects of p-chloroamphetamine and related drugs on central serotonergic mechanisms. *J. Pharmac. exp. Ther.* **192:** 33–41, 1975.
25. Sanders-Bush, E., D. A. Gallager and F. Sulser. On the mechanism of brain 5-hydroxytryptamine depletion by p-chloroamphetamine and related drugs and the specificity of their action. In: *Advances in Biochemical Psychopharmacology* Vol. 10, edited by E. Costa, G. L. Gessa and M. Sandler. New York: Raven Press, 1974, pp. 185–194.
26. Sheard, M. H. The effect of p-chloroamphetamine on single raphe neurons. In: *Advances in Biochemical Psychopharmacology*, Vol. 10, edited by E. Costa, G. L. Gesa and M. Sandler. New York: Raven Press, 1974, pp. 179–184.
27. Sheard, M. H. and M. Davis. p-Chloroamphetamine: short and long term effects upon shock-elicited aggression. *Eur. J. Pharmac.* **40:** 295–302, 1976.
28. Stein, J. M., M. J. Wayner and H. A. Tilson. The effect of parachlorophenylalanine on the intake of ethanol and saccharin. *Pharmac. Biochem. Behav.* **6:** 117–122, 1977.
29. Stein, J. M., M. J. Wayner, R. C. Cook and H. A. Tilson. The effect para-chloroamphetamine on the intake of ethanol, saccharin, food and water. In: *Currents in Alcoholism*, Vol. 3, edited by F. Seixas. New York: Grune and Stratton, 1977, in press.
30. Steranka, L. and E. Sanders-Bush. Temporal effects of p-chloroamphetamine on catecholamine synthesis. *Eur. J. Pharmac.* **45:** 83–86, 1977.
31. Strada, S. J. and F. Sulser. In vivo release of norepinephrine in the hypothalamus: Modification by p-chloroamphetamine and amphetamine. *Fedn Proc.* **29:** 417, 1970.
32. Trulson, M. E., E. E. Eubanks and B. L. Jacobs. Behavioral evidence for supersensitivity following destruction of central serotonergic nerve terminals by 5,7-dihydroxytryptamine. *J. Pharmac. exp. Ther.* **198:** 23–32, 1976.
33. Vorhees, C. V., G. J. Schaefer and R. J. Barrett. p-Chloroamphetamine: behavioral effects of reduced cerebral serotonin in rats. *Pharmac. Biochem. Behav.* **3:** 279–284, 1975.