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EFFECTS OF CHLORDIAZEPOXIDE ON PUNISHED AND UNPUNISHED RESPONDING BEFORE AND DURING CHLORDIAZEPOXIDE DRINKING. D.E. McMillan and J.D. Leander. Dept. of Pharmacol., Sch. of Med., Univ. of N.C., Chapel Hill, N.C. 27514

Rats were trained to lever press for food under a multiple fixed-interval 100 sec, fixed-interval 100 sec schedule, where responses during one component were punished with electric shock. A 10 mg/kg dose of chlordiazepoxide increased punished responding, but 3 and 30 mg/kg doses had little effect. The 3 and 30 mg/kg doses of chlordiazepoxide did not affect unpunished responding, but 30 mg/kg decreased the rate. Subsequently, a 0.5 mg/ml solution of chlordiazepoxide hydrochloride replaced the drinking water on the rats' home cages. After 7 weeks of drinking chlordiazepoxide, the chlordiazepoxide dose-effect curve was redetermined in these rats, who were averaging a daily intake of about 50 mg/kg of chlordiazepoxide. Drinking chlordiazepoxide about doubled the rate of punished responding, but did not affect unpunished responding. In the rats drinking chlordiazepoxide, injections of chlordiazepoxide increased both punished responding (3-100 mg/kg) and unpunished responding (3-30 mg/kg) across a wide range of doses. The increases in rates of punished responding were larger in the chlordiazepoxide drinkers, than they were before chlordiazepoxide was placed in the drinking water. (Supported in part by Grant #DA00570 from NIDA).

DRUG ABUSE

THURSDAY, AUGUST 25, 1977—9:00 A.M.

Law Building, Room 201

Cochairmen: Anthony T. Dren and Donald M. Thompson

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THE DISPOSITION OF ^3H - Δ^9 -TETRAHYDROCANNABINOL AND ^{14}C - Δ^9 -TETRAHYDROCANNABINOL. A.J. Siemens* and G.T. Pryor*. (SPON: C.M. Smith). Res. Inst. on Alcoholism, Buffalo, N.Y. 14203 and Stanford Res. Inst., Menlo Park, Calif. 94025.

Two laboratories have demonstrated that ^{14}C disappeared much more rapidly than ^3H from fresh blood of male Fischer and Wistar rats after intragastric administration of ^{14}C -labelled Δ^9 -tetrahydrocannabinol (THC) plus ^3H -THC at a total dose of 10 mg/kg. The disappearance rate was not different when blood samples were air dried before isotope analysis. At 24 hours after drug administration the concentration of ^3H was also higher than ^{14}C in fresh but not in lyophilized organs. The ^3H recovered in the lyophilizer condensate was distilled at 100°C. We postulate that ^3H -water was derived metabolically from the ^3H in the pentyl side chain of THC. In contrast, ^{14}C -THC plus ^3H -THC, 3 mg/kg, injected i.v. into bile duct-cannulated rats resulted in slightly higher ^{14}C than ^3H levels in blood and urine but higher ^3H than ^{14}C levels in bile. At 4 hours ^3H levels were higher than ^{14}C in the brain, the reverse occurring in the liver, lungs and heart. Drying of samples did not influence isotope concentrations after THC i.v. Total levels of ^{14}C and ^3H do not provide equivalent information on the disposition of THC. Supported by NIDA grant R01-DA-01136 & contract HSN-42-72-182.

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THE EFFECT OF Δ^9 -TETRAHYDROCANNABINOL ON FIRING PATTERNS OF THERMOSENSITIVE UNITS IN THE PREOPTIC REGION. William T. Schmelting* and Michael J. Hosko. Med. Col. of Wisconsin, Milwaukee, Wisconsin 53233.

Previous evidence from this laboratory has demonstrated a role for the preoptic region (POR) of the anterior hypothalamus in modulating Δ^9 -tetrahydrocannabinol (Δ^9 -THC) induced hypothermia. In order to specify this role, POR thermosensitive neurones were studied using extracellular techniques. Double wall stainless steel thermodes were stereotactically implanted bilaterally in POR. A thermocouple monitored POR temperature; tungsten microelectrodes were used to record single cell activity. Deep core temperature was monitored and maintained constant. Of all units studied to date 31% have been found to be hot or cold thermosensitive by accepted criteria ($Q_{10} > 2.0$). High primary thermosensitivities (T.S.) (Δ firing rate/ $^{\circ}\text{C}$) of > 6.0 ($Q_{10} > 5$) were found in 13.0% of the units. These units were challenged by Δ^9 -THC administration. Small doses (0.5-2.0 mg/kg) of Δ^9 -THC effectively altered the firing patterns of such units. Characteristically, spontaneous firing decreased while the T.S. of units to heating and cooling were differentially changed by Δ^9 -THC. [Supported by NIH Grant DA00124 and NIH Predoctoral Fellowship DA05072 (WTS).]