Acute and Chronic Effects of Δ⁹-Tetrahydrocannabinol on Food Intake by Rats

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Received April 18, 1974; Final Version July 16, 1974

Abstract. The effects of intraperitoneally injected Δ⁹-tetrahydrocannabinol (THC) were compared with d-amphetamine sulfate (d-AMP) on food intake in rats which were given access to food for 6 hrs each day. Food intake was markedly reduced in a dose-related fashion by THC (2.5 and 5.0 mg/kg) in the first 2 hrs after drug administration. This anorexic effect persisted for the next 4 hrs and even on the next day. The anorexic potency of d-AMP (1.25 and 2.5 mg/kg) was approximately twice that of THC in the initial 2-hrs interval after a single dose, but during the next 4 hrs and on the next day there was a compensatory increase in food consumption. Daily administration of THC (2.5 mg/kg) for 9 days greatly decreased food intake and body weight gain of animals which were injected immediately before feeding, but had little effect on animals injected 16 hrs before feeding.

Keywords: Δ⁹-Tetrahydrocannabinol (THC) — d-Amphetamine Sulfate (d-AMP) — Food Intake by Rats — Acute and Chronic Dosing — Anorexic Drug Effect.

Evidence is incomplete and somewhat conflicting about effects of crude marihuana extract or Δ⁹-tetrahydrocannabinol¹ (THC), its major psychoactive constituent (Burstein, 1973), on food intake by laboratory animals. Single doses of THC or of several analogs substantially decreased food intake by animals deprived of food 24 hrs prior to intraperitoneal administration of THC. However, in studies on rats and pigeons (Boyd et al., 1963; McMillan et al., 1971) the drug effect on the operant response required to obtain food could not be distinguished from the drug effect on the consummatory response. In another study on rats, measuring food consumption only, Glick and Milloy (1973) reported that food consumption increased following a lower dose of THC (1.0 mg/kg) and decreased following a higher dose (2.0 mg/kg).

Several investigators (Borgen et al., 1971; Elsmore and Fletcher, 1972; Manning et al., 1971; Phillips et al., 1972; Järbe and Henriksson,

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¹ An alternative to this formal numbering for the same compound is the monoterpenoid numbering, Δ⁹-tetrahydrocannabinol.
1973; Sjödén et al., 1973) have shown decreases in food consumption and body weight following daily administration of THC with doses ranging from 4 to 200 mg/kg. Abel and Schiff (1969) have found the same effect with the THC analog, pyrahexyl 15.0 mg/kg. However, food consumption was measured only 24 hrs after each daily administration of the drug so that any brief, acute drug effects were not measured. The continuous availability of food limited the findings to a condition of continuous satiation or minimal hunger. In addition, the THC effect on food intake was not compared with d-amphetamine or any other standard anorexic drug.

The present study was designed to compare directly the effects of THC and d-amphetamine sulfate (d-AMP), a clinically useful anorexic drug, on food intake by rats which had access to food for 6 hrs each day. In addition, chronic effects of THC were subsequently tested in the same rats.

**Methods**

*Animals and Preliminary Training.* The subjects were 30 male, albino rats (Wistar descendants obtained from Hilltop Lab Animals, Inc., Scottsdale, Pennsylvania U.S.A.) weighing 150 to 180 g at the start of the training. Each rat was housed individually in standard cages (wire mesh floor with three sides of solid stainless steel and a wire mesh front) and supplied with water continuously. The laboratory environment consisted of automatically controlled illumination with 12 hrs of light (6 a.m. to 6 p.m.) alternating with 12 hrs of dark (6 p.m. to 6 a.m.) and temperature regulated at 22–24°C.

Each rat received standard laboratory food (Purina Lab Chow Checkers) on the floor of its cage for a 6-hrs period each day (8 a.m. to 2 p.m.), thus being trained to consume its daily solid food intake within this time interval. The amount of food given, which almost always exceeded consumption, was 20 g for the first 28 days and 35 g thereafter. Throughout the entire experiment water was continuously available to all animals. Cohen (1966) previously used the same feeding schedule to test anorexic effects of anticholinergic agents. Spengler and Waser (1959) and LeDouarec et al. (1966) used a very similar schedule with 7 instead of 6 hrs of daily food availability to test anorexic effects of d-AMP and other drugs.

Drug tests were begun after a baseline period of 28 days, whereas Cohen (1966) limited the pre-drug baseline to 3 days. The 26 rats remaining alive from the original group of 30 were divided into 2 groups of 6 each and 2 groups of 7 each.

*Drugs.* The drug doses were administered intraperitoneally (i.P.) in a volume of 1.0 ml/kg of body weight. The vehicles were undiluted propylene glycol for THC, as described by Sofia et al. (1973), and distilled water for d-AMP. All control injections contained the same volume of the vehicle.

*Procedure.* The same animals were used in two stages, the first testing acute drug effects and the second testing chronic drug effects. In the first stage each drug and its vehicle were administered once a week for a total of 8 weeks according to an experimental design which varied the sequence of drugs and included both drugs and their vehicles in each weekly test. Four subgroups were established and the following sequence of treatments assigned in the first 2 weeks: (a) vehicle, THC; (b) THC, vehicle; (c) d-AMP, vehicle; and (d) vehicle, d-AMP. In the next