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Intragastric Methylphenidate Does Have Effects On The Behavior of Rats[1]

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FOLTIN, R. W. *Intragastric methylphenidate does have effects on the behavior of rats.* PHARMAC. BIOCHEM. BEHAV. 17(5) 1089–1090, 1982.—The effects of intraperitoneal (2.0–32 mg/kg) and intragastric (8.0–96 mg/kg) methylphenidate on milk intake were determined in two groups of rats. Experimental sessions consisted of 15 min access to a sweetened milk solution each day, seven days a week. Following the determination of baseline intake, a dose of methylphenidate was administered prior to the session once every four days with all rats in each group receiving all doses. Although methylphenidate was equally effective in decreasing milk intake using either route of administration, intraperitoneal methylphenidate was four times as potent as intragastric methylphenidate.

Methylphenidate Behavior Milk intake Rats

A RECENT paper [5] compared the effects of methylphenidate (MP) and *d*-amphetamine on locomotor activity (LMA) following intraperitoneal (IP) and oral administration. Intraperitoneal *d*-amphetamine was more potent than oral *d*-amphetamine and *d*-amphetamine by either route of administration was more potent than IP methylphenidate in increasing LMA. However, oral MP was reported to have no effect on LMA. The greater potency of parenteral versus oral *d*-amphetamine has been reported in several species including monkeys [2], mice [1], and rats [3].

The failure of oral MP to effect LMA is puzzling since humans are administered this drug orally [4]. However, since the recent paper [5] used the same two doses of each drug for each route of administration rather than determining complete dose-response functions that study does not provide accurate information about efficacy or potency. In the present study, the effects of intragastric (IG) and intraperitoneal MP on milk consumption were determined in rats. Intragastric MP was found to be less potent than intraperitoneal MP in decreasing milk intake, but MP was equally efficacious using either route of administration.

METHOD

Animals and Apparatus

Twenty-four male Sprague-Dawley rats (Holtzman, Madison, WI) weighing between 250 and 300 g at the start of the experiment were individually housed in standard ceiling-suspended stainless steel cages with water available ad lib except during the experimental sessions. Sweetened condensed milk (Borden's CO., Columbus, OH; 1:2, milk: tap water) was presented in Wahmann (Baltimore, MD) 100 ml calibrated bottles attached centrally to the front of the cages. Supplemental feedings of 4–6 g of rat chow (4% mouse and Rat Diet, Teklad, Winfield, IA) were given following each experimental session. A 6:00 a.m. to 6:00 p.m. light-dark cycle was maintained in the colony room with a constant temperature of 22°C.

Procedure

Experimental sessions consisting of a single 15 min presentation of milk occurred daily (10:00–10:15 a.m.), seven days a week. Following stabilization of milk intake (less than 10% variation in mean intake for three consecutive sessions) animals were randomly assigned to one of two groups, with each group containing 12 rats. One group received IP physiological saline injections given 15 min prior to the session, while the other group received IG physiological saline infusions given 30 min prior to the session for four consecutive sessions. A longer pretreatment time was used for the IG route due to the possibility of slower absorption from the gastrointestinal tract. For intragastric infusions, the rats were held in one hand with the mouth held open by a wire mouthpiece and an 8 cm tube (2.5 mm o.d. × 1.5 mm i.d.) was gently passed down the espophagus to the stomach. Dose response functions for MP (2–32 mg/kg, IP; 8–96 mg/kg, IG) were then determined. Doses were administered in random order with all animals in one group receiving all doses intragastrically and all animals in the other group receiving all doses intraperitoneally with at least three days of stable milk intake separating drug administrations.

Drug

Methylphenidate hydrochloride (CIBA Pharmaceutical Co., Summit, NJ) was dissolved in physiological saline with

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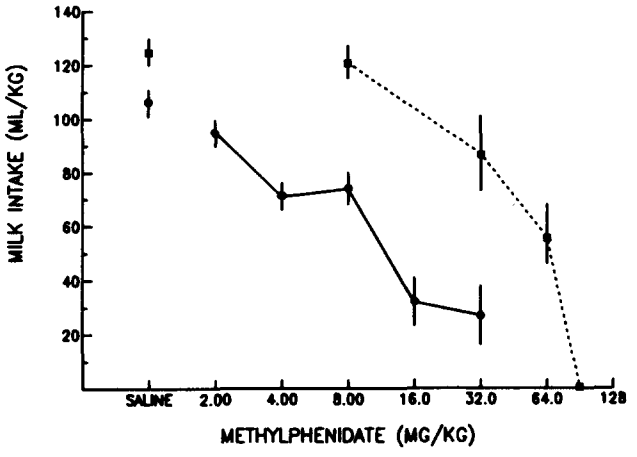

FIG. 1. Mean milk intake and SEMs as a function of dose of methylphenidate following IP, ●—●, and IG, ■---■ administration.

a constant infusion volume of 1 ml/kg. Doses are expressed as weight of the salt.

RESULTS

During the determination of baseline milk intake one of the rats in the IG group developed an ear infection and was removed from the study. Milk intake stabilized in 14 to 17 days for both groups at about 110 ml/kg. As shown in Fig. 1 both IP and IG methylphenidate produced dose-dependent decreases in milk drinking with the IG dose-response function shifted to the right of the IP dose-response function. The ED 50 with 95% confidence interval as determined by linear regression following IP administration was 9.4 mg/kg (7.4–12.0 mg/kg) and following IG administration it was 38.9 mg/kg (30.2–50.0 mg/kg).

DISCUSSION

The effects of methylphenidate on milk drinking were determined following IP and IG administration in rats. Intraperitoneal administration was found to be four times more potent than IG, but the drug was equally efficacious in decreasing milk intake using either route of administration. These results disagree with an earlier study [5] that reported oral MP to be without effect on LMA in rats. However, in that study the largest dose of MP administered was only 6.4 mg/kg. Clearly, the dose range tested in the previous study [5] was not wide enough to validate the authors' conclusion that oral MP is ineffective. The use of a wide range of doses in the present study allowed the accurate comparison of the efficacy and potency of MP when administered by the IG or IP route. Thus, the determination of complete dose-response functions is essential for the analysis of the behavioral effects of drugs.

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