DELTA-9-TETRAHYDROCANNABINOL (THC) FAILS TO STIMULATE CONSUMPTION OF A HIGHLY PALATABLE FOOD IN THE RAT

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Abstract: THC is the active chemical component in marijuana. In humans, it is known to cause acute sedation, alterations of cognition, and to stimulate appetite. The goal of this study was to determine if THC would produce acute stimulation of the consumption of a highly-palatable food item in the rat. Separate groups of rats were administered THC (1.0 or 2.0 mg/kg) either 30, 60, or 120 min prior to being placed in the presence of a highly palatable food (Nilla Wafers soaked in water). Spontaneous exploration decreased at the 2.0 mg/kg dose of THC at the 60 min time point. The amount of food eaten was not significantly changed at either dose. These results do not support the hypothesis that THC causes acute appetite stimulation in the rat. However, some other non-specific effect of THC that indirectly reduced food consumption without directly acting upon appetite is a possible explanation that cannot be presently excluded, and that will need to be assessed in future studies. © 1998 Elsevier Science Inc.

Key Words: anandamide, appetite, cannabinoid, marijuana

Introduction

Delta-9-tetrahydrocannabinol (THC) is the primary psychoactive chemical component in marijuana. It is known to cause acute stimulation of appetite in humans (1,6), and in low doses has been used as an anti-emetic and appetite stimulant for persons in chemotherapy, who are anorexic, or who have AIDS (8). In contrast, studies in rats have shown inconsistent effects of THC on feeding, where both stimulation (e.g. 2) and suppression (e.g. 4,9) have been produced.

What may underlie these discrepancies is that there are two distinct human phenomena that could be modeled in the rat. Previous studies in rats employed procedures where testing occurred in the home cage, at moderate to long time points, and which were concerned with the overall patterns of ingestion (2,4,9). This work would be most useful for assessing therapeutic uses of cannabinoids, where long-lasting appetite stimulation is desirable. In contrast, acute stimulation of appetite in satiated humans might be better modeled by assessing the short-term ingestion of a highly-palatable food in satiated animals. Therefore, the goal of the present study was to determine if THC would produce acute stimulation of the consumption of a highly-palatable food item in the rat.

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For the present study, we chose to use the Nabisco Nilla Wafers™ as the food item, because it is a high fat and high calorie food, the baseline intake is high, and the intake in rats of this food is substantially enhanced by administration into the hypothalamus of galanin and other neurochemicals thought to mediate the control of feeding (e.g. 3).

Methods

Subjects: Thirty-one male Sprague-Dawley rats (Taconic Farms, Germantown, NY) were housed individually in a temperature controlled room of 20-22 C under a normal 12-hr light-dark cycle. During periods of behavioral testing, the subjects were maintained on free access to lab chow and water. Body weights were taken before and after the experiment to ensure that animals did not experience any substantial weight change around the time of the testing.

Drug Preparation: THC (obtained as a gift from NIDA) was received as a resin dissolved in ethanol. Stock injection concentrations were prepared by first mixing the THC with equal parts of emulphor (GAF, Rochester, NY), then normal saline was added slowly to produce an injection solution.

Apparatus and Procedures: Activity was measured in a standard Digiscan Automated Activity Monitor (Omnitech Electronics, Columbus, OH). THC (1.0 or 2.0 mg/kg i.p., 0.1 ml/kg rat) was administered to six separate groups (a 2 x 3 design where N=4 for each group) of rats either 30, 60, or 120 minutes prior to being placed in the Digiscan apparatus in the presence of two Nabisco Nilla Wafers™ (Nabisco Brands, Inc. East Hanover, N.J.; %wt: fat = 14%, carbohydrate = 79%, protein = 7%) cookies, soaked in 10 ml water, in a plastic weighing boat. One additional group (N=7) received saline i.p. (0.1 ml/kg rat) 30 minutes prior to being placed in the presence of the cookies in the Digiscan. Only the 30 min time point was chosen for the saline group because no performance difference of saline administered at different time points was expected. The sessions, during which activity and food consumption were simultaneously measured, were 20 min in duration. All animals were pre-exposed to one cookie in the homecage 48 hours prior to the experiment. All subjects consumed the cookie entirely within a 24 hour period.

The doses of THC were chosen to expose the rats to doses known to be intermediate along the range of possible effective doses (7). Previous feeding studies used doses that were in the range known to produce a reduction of activity. For example, suppression of feeding was shown at doses in the ranges of 2.0-5.0 mg/kg (4, 9). In the way of further validation, the doses chosen for the present study were shown to produce impairments in the performance of rodent memory paradigms, without producing severe motor effects (5, 7). The three time points for the THC administration were chosen to assess the possibility that the point of greatest stimulation of feeding would be as the initial, acute effects of THC diminished.

Results

Figure 1 shows the effects on spontaneous activity (Panel A) and food consumption (Panel B) of two doses of THC at three post-injection time points. The 2.0 mg/kg dose of THC produced a significant reduction in ambulations, as indicated by a significant interaction in the ANOVA (Dose x Time interaction: F2,24=3.53, p<.04). A t-test comparing the 2.0 mg/kg group at the 60 min post-injection time point versus the saline group was significant (p<.03). No dose of THC produced a significant effect on food consumption.
The effects on spontaneous activity (Panel A) and food consumption (Panel B) of two doses of THC at three post-injection time points. Shown are the means ± s.e.m.
Discussion

The present study sought to determine if THC would produce acute stimulation of the consumption of a highly-palatable food item in the rat. The lack of feeding stimulation at the 1.0 mg/kg dose suggests that motor impairment cannot solely account for this lack of effect. We observed that THC produced a small reduction in motor activity at the higher 2.0 mg/kg dose, but not at the smaller 1.0 mg/kg dose. Neither dose stimulated feeding. However, some other non-specific effect of THC that indirectly reduced food consumption without directly acting upon appetite is a possible explanation that cannot be presently excluded.

One concern that could be raised is that the failure to see a stimulation of feeding resulted from a ceiling effect. However, the amounts consumed by the saline control group and several of the THC groups in the present study, approximately 2.0 g in 20 min, were very close in other published reports using this same Nilla Wafer paradigm (e.g. 3). Additionally, stimulated-feeding groups in other studies often consume approximately 8-10 g in the 20 min test period, demonstrating that the ceiling for this paradigm is considerably higher than 2.0 g of food consumed (3).

Another criticism that might be made is that the present study lacked sufficient statistical power to detect positive stimulation of feeding because of the small number of subjects in each group. This criticism would be of special concern if a trend toward a stimulation of feeding was evident. However, in fact, a non-significant trend toward a reduction of feeding was evident instead, making it unlikely that a larger number of subjects per group would reveal significant stimulation of feeding.

This failure to find acute feeding stimulation in the present study may reflect a difference between humans and rats in the role that endogenous cannabinoids play in regulating appetite. This is an intriguing hypothesis to consider in future comparative studies of the neurobiology of food intake regulation, and perhaps represents a limitation of using rodent models of stimulated-food intake for the screening of novel cannabinoid or anandamideergic pharmaceuticals.

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References