ELSEVIER

Physiology & Behavior 86 (2005) 475 – 479

PHYSIOLOGY & BEHAVIOR

Effect of Δ^9-tetrahydrocannabinol on sucrose palatability as measured by the taste reactivity test

Maegan M. Jarrett, Cheryl L. Limebeer, Linda A. Parker *

Department of Psychology, Wilfrid Laurier University, Waterloo, Ontario, Canada, N2L 3C5

Received 3 May 2005; received in revised form 25 July 2005; accepted 1 August 2005

Abstract

The taste reactivity test was employed to determine the effect of pre-treatment with Δ^9-Tetrahyrdrocannabinol THC on sucrose palatability. In Experiment 1, on each of 9 trials, rats were injected with THC or Vehicle prior to receiving a 5 min intraoral infusion of sucrose solution. The concentration of sucrose (2%, 10% or 32%) and the interval between the injection and the sucrose infusion (30, 60 or 120 min) were varied in a within-subjects design. THC enhanced the frequency of ingestion reactions only when administered 120 min prior to the taste reactivity test, regardless of sucrose concentration. In Experiment 2, the CB_1 antagonist, SR141716, reversed the enhanced sucrose palatability produced by THC. These results suggest that the increased intake of palatable food 2 h, but not earlier, following administration of a low dose of THC may be the result of enhanced palatability and that this effect is the result of action of THC at the CB_1 receptor.

Keywords: Cannabinoid; Feeding; Liking; Taste reactivity; THC; Sucrose; Rat

It is well known that humans report an increased appetite, particularly for sweet foods, within 3 h after smoking marijuana [1–4]. Recently, considerable advances have been made towards understanding the mechanisms responsible for this effect [5]. Although the psychoactive component of marijuana, Δ^9-Tetrahyrdrocannabinol (THC) was discovered over 40 years ago [6], it is only in the past decade that the mechanism of action of THC within the Central Nervous System (CNS) has been discovered. THC acts at cannabinoid (CB_1) receptors, to which the endocannabinoids, anandamide, 2-arachidonylgycerol (2-AG) and noladin ether, bind [7–10].

There is considerable experimental evidence for a role of the cannabinoid system in the regulation of food intake and appetite [11–16]. Low to moderate doses (0.5 and 1 mg/kg) of THC produce acute hyperphagia in deprived or presatiated rats [12–16]. Williams et al. [14] found that pre-fed rats who were treated with a moderate dose of THC (0.5 or 1.0 mg/kg) consumed significantly more rat chow than those treated with higher doses (2.0 mg/kg) or lower (0.063–0.25 mg/kg) doses. Hyperphagia was obtained even though all of the rats had been presatiated with palatable food. Similar results were obtained in a later study by Koch [13] which investigated whether THC-induced hyperphagia would be influenced by diets high in fat and sugar. After injecting the rats with THC, non-deprived animals were exposed to one of three diets (rat chow, high-fat and sweetened high-fat). Moderate doses of THC (0.5 or 1.0 mg/kg), but not higher doses (2.5 mg/kg), increased the intake of all diets; however, the largest increases in intake were found in rats fed both the high-fat and the sweetened high-fat diets.

The mechanism involved in THC-induced increase in appetite is not known, however, there are two prominent hypotheses: 1) cannabinoids affect the appetitive or incentive aspects of feeding behavior, 2) cannabinoids affect the palatability of the food. In support of the appetite hypothesis, THC produces a marked reduction in latency to begin eating [15,17] and the CB_1 receptor agonist, CP 55,940, causes rats to work harder to obtain sucrose or beer on a progressive ratio licking schedule [18]. Conversely, CB_1 antagonists reduce rates of responding for food or fluids [19–22]. These effects suggest that endocannabinoid activity may be linked to the appetitive phase of responding by increasing the incentive value of food stimuli. On the other hand, there is also support for the hypothesis that manipulation of the endocannabinoid system modifies palatability directly. Low doses of THC selectively

* Corresponding author. Tel.: +1 519 884 0710 3900; fax: +1 519 746 7605.
E-mail address: lparker@wlu.ca (L.A. Parker).

0031-9384/$ - see front matter © 2005 Elsevier Inc. All rights reserved.
doi:10.1016/j.physbeh.2005.08.033

enhance intake of palatable foods and fluids [14,23–25] and blockade of CB_1 receptors selectively suppresses intake of palatable foods [11,26]. Most recently, using microstructural analyses of licking of a 10% sucrose solution, Higgs et al.[12] reported that THC and the endogenous cannabinoid, anandamide, significantly increased the total number of licks by increasing the duration of bouts of licking as well as increasing the asymptote of cumulative lick curve, effects consistent with increases in palatability [27].

The evaluation of the effect of THC on palatability has relied exclusively upon intake measures that include both appetitive and consummatory phases of responding [e,g,Ref,28]. Appetitive behaviors are associated with the animal's approach to the spout, whereas consummatory behaviors are associated with drinking the solution. Appetitive behaviors can be affected by variables other than palatability. A more direct measure of the palatability is the taste reactivity (TR) test developed by Grill and Norgren [29]. In the TR test, a flavored solution is infused directly into the intraoral cavity of the rat's mouth via an implanted intraoral cannula. Upon infusion of a tastant the rat will displays a characteristic set of orofacial and somatic responses that reflects the palatability of the solution. Palatable solutions, such as sucrose, elicit ingestive TR behaviors (tongue protrusions and mouth movements) where as aversive solutions, such as quinine, will elicit rejection TR patterns (primarily gaping) [29]. The present experiments evaluated the effect of THC on the palatability of sucrose solution employing the taste reactivity (TR) paradigm. A single low dose of THC (0.5 mg/kg) was employed, because previous studies have demonstrated that higher doses of the drug can produce aversive effects [e,g,30,31]. It has been suggested that a low dose of 0.5 mg/kg produces blood levels within the range that humans might experience after smoking 1–2 marijuana cigarettes [17,32]. The effect of this low dose of THC on the palatability of 3 concentrations of sucrose (2%, 10% and 32%) was assessed.

The interval between THC administration and sucrose infusion (30, 60 and 120 min) was also varied. Within 3 h after smoking marijuana, recreational users report an increased appetite, especially for sweet foods [1,3]. In Experiment 2, the potential of the CB_1 receptor antagonist, SR141716, to reverse the modification of sucrose palatability by THC was evaluated.

1. Method

1.1. Subjects

Subjects were male Sprague–Dawley rats weighing between 250 and 350 g at the beginning of the experimental testing (Charles River Laboratories, St. Constant, Quebec). The rats were maintained on ad libitum rat chow and water throughout the duration of the experiment, with the exception of testing in the TR chamber. All of the rats were housed individually in hanging wire mesh cages. The rats were kept in temperature and humidity-controlled room on a 12 : 12 h light–dark schedule with lights on at 0700 h. All experimental procedures occurred in the light phase of the rat's daily activity cycle. All procedures were approved by the Wilfrid Laurier University Animal Care Committee in accordance with the guidelines of the Canadian Council on Animal Care.

1.2. Surgery

The rats were surgically implanted with intraoral cannulae as described by Limebeer and Parker [33]. Prior to beginning the surgical procedure the animals were anesthetised using isoflurane gas and given a subcutaneous injection of anafen (7 mg/kg) as an anti-inflammatory agent. Once the animal had been anesthetised, a 15-g thin-walled stainless steel needle was inserted in the midneck region and moved subcutaneously below the ear and brought out behind the first molar inside the mouth. Intramedic polyethylene tubing was inserted into the cheek and the needle was removed. The tubing was held in place by an anchoring on the inside of the cheek and on the tubing exiting the midneck region. The rats were allowed to recover for 1 week before any experimental procedures were conducted.

1.3. Apparatus

The testing chamber was composed of Plexiglas ($22.5 \times 26 \times 20$ cm) with a Plexiglas top. The rat's cannulae were attached to an infusion pump (Harvard Apparatus, South Natick, MA) through the ceiling of the chamber. During the 5 min infusion, the rat's orofacial and somatic responses were videotaped using a Canon Digital Camera with a telephoto lens from a mirror mounted at a 45° angle beneath the test chamber [33].

1.4. Drugs

The Δ^9-Tetrahydrocannabinol, obtained from the National Institute of Drug Abuse (NIDA), was prepared in a solution of 1 ml ethanol, 1 ml Cremaphor (Sigma) and 18 ml saline at a concentration of 1 mg/ml. The rats were injected with 0.5 ml/kg (0.5 mg/kg). SR141716, obtained from NIDA, was prepared in the same Vehicle as THC at a concentration of 2.5 mg/ml and injected in a volume of 1 ml/kg. The drugs were always administered intraperitoneally.

1.5. Procedure

1.5.1. Experiment 1: THC alone

To familiarize the rats with the sucrose solution, for 5 days prior to surgery the rats received continuous access to 32% sucrose solution as well as their ad lib water. In order to attenuate the novelty of the drug which may contribute to its aversive properties, all rats received a preinjection of 1 mg/kg of THC, 72 h prior to the beginning of TR testing [34].

On the day prior to TR testing, the rats received an adaptation trial in the TR chamber. On this trial each rat's cannula was attached by tubing to an infusion pump (Harvard Apparatus) which delivered the water at a rate of 1 ml/min for 5 min duration.