Neuroscience 167 (2010) 439–455

DIFFERENTIAL EFFECTS OF DOPAMINE AND OPIOID RECEPTOR BLOCKADE ON MOTIVATED COCA-COLA DRINKING BEHAVIOR AND ASSOCIATED CHANGES IN BRAIN, SKIN AND MUSCLE TEMPERATURES

E. A. KIYATKIN*

Behavioral Neuroscience Branch, National Institute on Drug Abuse – Intramural Research Program, National Institutes of Health, DHHS, 333 Cassell Drive, Baltimore, MD 21224, USA

Abstract—Although pharmacological blockade of both dopamine (DA) and opiate receptors has an inhibiting effect on appetitive motivated behaviors, it is still unclear which physiological mechanisms affected by these treatments underlie the behavioral deficit. To clarify this issue, we examined how pharmacological blockade of either DA (SCH23390+eticlopride at 0.2 mg/kg each) or opioid receptors (naloxone 1 mg/kg) affects motor activity and temperature fluctuations in the nucleus accumbens (NAcc), temporal muscle, and facial skin associated with motivated Coca-Cola drinking behavior in rats. In drug-free conditions, presentation of a cup containing 5 ml of Coca-Cola induced locomotor activation and rapid NAcc temperature increases, which both transiently decreased during drinking, and phasically increased again after the cup was emptied. Muscle temperatures followed this pattern, but increases were weaker and more delayed than those in the NAcc. Skin temperature rapidly dropped after cup presentation, remained at low levels during consumption, and slowly restored during post-consumption behavioral activation. By itself, DA receptor blockade induced robust decrease in spontaneous locomotion, moderate increases in brain and muscle temperatures, and a relative increase in skin temperatures, suggesting metabolic activation coupled with adynamia. Following this treatment (~180 min), motor activation to cup presentation and Coca-Cola consumption were absent, but rats showed NAcc and muscle temperature increases following cup presentation comparable to control. Therefore, DA receptor blockade does not affect significantly central and peripheral autonomic responses to appetitive stimuli, but eliminates their behavior-activating effects, thus disrupting appetitive behavior and blocking consumption. Naloxone alone slightly decreased brain and muscle temperatures and increased skin temperatures, pointing at the enhanced heat loss and possible minor inhibition of basal metabolic activity. This treatment (~60 min) had minimal effects on the latencies of drinking, but increased its total duration, with licking interrupted by pauses and retreats. This behavioral attenuation was coupled with weaker than in control locomotor activation and diminished temperature fluctuations in each recording location. Therefore, attenuation of normal behavioral and physiological responses to appetitive stimuli appears to underlie modest inhibiting effects of opiate receptor blockade on motivated behavior and consumption. Published by Elsevier Ltd on behalf of IBRO.

*Corresponding author. Tel: +1-443-740-2844; fax: +1-443-740-2155.
E-mail address: ekiyatki@intra.nida.nih.gov (E. A. Kiyatkin).
Abbreviations: DA, dopamine; NAcc, nucleus accumbens; THC, 9-tetrahydrocannabinol.

0306-4522/10 $ - see front matter. Published by Elsevier Ltd on behalf of IBRO.
doi:10.1016/j.neuroscience.2010.02.032

Key words: brain metabolism, dopamine antagonists, naloxone, neural activation, motivation, reward.

It is known that pharmacological blockade of dopamine (DA) receptors has a powerful inhibiting effect on different types of motivated behaviors established by positive and negative reinforcers (Le Moal and Simon, 1991; Wise and Bozarth, 1987); the effect is especially strong with respect to drinking and feeding behaviors (Dourish, 1983). Appetitive motivated behaviors are also affected by the blockade of opiate receptors; these effects are less robust, more delicate, but also are especially evident with respect to consumption of palatable foods and drinks (Bolles and Fanselow, 1982; Cleary et al., 1996; Holloway et al., 2004; Brown and Holtzman, 1981). While these data suggest that both DA and endogenous opioid peptides are involved in organization and performance of motivated behavior, a highly energetic debate is continued for the last 30 years to define this role in psychological terms (Barbano and Cador, 2006, 2007; Beninger, 1983; Berridge, 1996; Berridge and Robinson, 1998; Di Chara, 2002; Hayward et al., 2002; Kelley et al., 2005; Robbins and Everitt, 1996; Salamone et al., 1991; Salamone and Correa, 2002; Schultz et al., 1997; Schultz, 2002; Wise et al., 1978; Wise, 1982). This debate is based on enormous volume of experimental data that analyze animal behavioral output in different models (varying in nature and quality of the reinforcer, the means of its obtainment, animal homeostatic state, concomitant environmental conditions) and various types of genetic and pharmacological interventions. While this discussion has sparked from a famous “anhedonia hypothesis” (Wise et al., 1978; Wise, 1982) that explained the behavior-inhibiting effects of DA antagonists by their ability to reduce the affective or pleasurable actions of food and other rewards (i.e., to make them less reinforcing), further experimental evidences were more consistent with drug-induced deficits of motivational or preparatory aspects of appetitive behavior (Berridge and Robinson, 1998; Di Chara, 2002; Robbins and Everitt, 1996; Salamone et al., 1991, 2009; Salamone and Correa, 2002). In contrast, endogenous opioids were more implicated in the evaluation of the hedonic, pleasant effects of positive reinforcers that make them desired and wanted (Berridge, 1996; Hayward et al., 2002; Kelley et al., 2005; Barbano and Cador, 2007).

In the present study we explored another approach to examine the role of DA and endogenous opioid mecha-

nisms in appetitive motivated behavior by defining physiological mechanisms that are affected by DA and opioid receptor blockade and could underlie drug-induced behavioral deficit. As a behavioral model, we choose a simple paradigm of learned drinking of sugar-containing caffeine-free Coca-Cola®. Rats quickly establish Coca-Cola drinking after a few days of passive training and maintain this behavior for many repeated sessions without food and water deprivation. In addition to quantifying the latencies to initiate drinking and drinking durations, we examined the pattern of locomotor activity and temperature fluctuations in the brain (nucleus accumbens (NAcc)), facial skin and temporal muscle. These tests were conducted in both drug-free conditions and after systemic blockade of either opioid (naloxone 1 mg/kg) or DA (a mixture of D1- (SCH23390 0.2 mg/kg) and D2- selective (eticlopride 0.2 mg/kg)) antagonists. Therefore, we were able to evaluate how either treatment affects (a) basal motor activity and temperatures, (b) drinking behavior, and (c) temperature and motor effects associated with key events of drinking behavior. Temperatures were recorded with a high temporal resolution (5-s), allowing for the analysis of both tonic and phasic, event-related, temperature fluctuations.

Brain temperature is closely related to neural metabolism, reflecting a dynamic balance between metabolism-related heat production and heat loss by cerebral circulation to the rest of the body and then to external environment. In contrast to widespread beliefs on stability and tight regulation, brain temperature shows relatively large (~3 °C) and rapid (5–10 s) fluctuations associated with various environmental stimuli and occurring during different behaviors (see Kiyatkin, 2005, 2010 for review). While phasic increases in brain temperature primarily reflect metabolic neural activation, fluctuations in skin temperature provide a valuable measure of peripheral vasoconstriction—another sensitive, centrally mediated response triggered by various arousing and reinforcing stimuli (Baker et al., 1976). The temporal muscle is a non-locomotor head muscle that receives the same blood supply as the brain (via the carotid artery); this recording site is important for evaluating the contribution of arterial blood supply to alterations in brain and skin temperatures. Thus, simultaneous recordings of locomotion and temperature fluctuations in different central and peripheral locations in drug-free and treatment conditions could add new information on the effects of DA or opiate receptors blockade on basal physiological state and alterations in basic physiological mechanisms that underlie drug-induced behavioral deficit.

EXPERIMENTAL PROCEDURES

Subjects

Six Long-Evans male rats (Taconic, Germantown, NY), weighing 400–460 g and housed under a 12 h light cycle (lights on at 0700), with *ad libitum* food and water, were used. Prior to surgery, rats were put through a pilot trial of the Coca-Cola drinking procedure for both training and selective purposes (see below). Protocols were performed in compliance with the Guide for the Care and Use of Laboratory Animals (NIH, Publications 865–23) and were approved by the Animal Care and Use Committee, NIDA-IRP.

Surgery

All animals were implanted with three thermocouple electrodes as previously described (Kiyatkin and Brown, 2005). Animals were anesthetized i.p. with 3.3 ml/kg of Equithesin (sodium pentobarbital, 32.5 mg/kg and chloral hydrate, 145 mg/kg) and mounted in a stereotaxic apparatus. Four holes were drilled through the skull: three for securing screws and one for thermocouple insertion in the NAcc shell (1.2 mm anterior to bregma, 0.9 mm lateral to bregma) using the coordinates of Paxinos and Watson (1998). The *dura mater* was retracted and the thermocouple probe was slowly lowered to the desired target depth (7.4 mm, measured from the skull surface). A second thermocouple probe was implanted s.c. along the nasal ridge with the tip approximately 15 mm anterior to bregma. Although the tail is the primary organ of heat dissipation in rats, facial skin has dense vascularization and this location provides mechanical stability of the electrode, an essential condition for long-term, artifact-free temperature recordings. A third thermocouple probe was implanted in the deep temporal muscle (*musculus temporalis*), which has a similar arterial blood supply as the brain and not directly involved in motor activity. Because temperature fluctuations in skin and muscle depend upon two variables: the state of vessels (vasoconstriction/vasodilatation) and the temperature of arterial blood inflow, these two locations were important for evaluating the source of temperature fluctuations and their underlying mechanisms. By tracking temperature responses in different brain and body sites with a short collection interval, one is able to follow the dynamics of heat generation and flows within the organism. The probes were secured with dental cement to the three stainless steel screws threaded into the skull. Rats were allowed 3 days recovery and two more days of habituation (6 h sessions) to the testing environment before the start of testing.

Experimental protocol

During three training sessions that preceded surgeries, rats were placed in experimental chamber and, after 2–3 h habituation period, were given a container (a small plastic bottle cap, ~3.0×1.6 cm^2, fixed on a metal plate for stability) holding 5 ml of caffeine-free Coca-Cola Classic (Coke®). This drink contains 11% of sugars, with 1.97 calories or 0.55 g of sugars in a 5-ml portion. Coca-Cola samples were de-gassed by intense shaking and had temperature equal to room temperature (22–23 °C). The cup with Coca-Cola was presented for 1 h and the procedure was repeated twice during the ~6-h session. Rats were not food- or water-deprived before the sessions, but had no food or water except two Coca-Cola drinks each presented for 1-h intervals. If the rats learned to consume the beverage entirely during two consecutive presentations, they were selected for surgery. Three rats, which showed inconsistent Coca-Cola drinking were excluded from further work.

All tests occurred inside a Plexiglas chamber (32×32×32 cm^3) placed inside a sound- and light-attenuated plastic box (60×56×70 cm^3) under continuous weak white light insulation (15 W) and in view of a small video camera mounted above the cage. These chambers were equipped with four infrared motion detectors (Med Associates, Burlington, VT, USA), allowing for monitoring locomotor activity. Rats were brought to the testing chamber at ~09:30 AM and attached via a flexible cord and electrical commutator to thermal recording hardware (Thermes 16, Physitemp, Clifton, NJ, USA). Temperatures were recorded with a 5-s time resolution and movement was recorded as the number of infrared beam breaks per 1 min. Room temperature was maintained at 22–23 °C and controlled by another thermocouple located inside of the recording chamber.

During the first 2–3 recording sessions, each rat was exposed to a similar basic testing protocol, which included two presentations of 5 ml Coca-Cola samples. After 2–3-h habituation period

Download English Version:

https://daneshyari.com/en/article/6277640

Download Persian Version:

https://daneshyari.com/article/6277640

Daneshyari.com