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High versus low fat/sugar food affects the behavioral, but not the cortisol response of marmoset monkeys in a conditioned-place-preference task

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HIGHLIGHTS

- Consumption of chocolate induced a CPP effect in the marmosets.
- CPP was associated with foraging time, not amount of calories ingested.
- The CPP response was not predicted by baseline behaviors or cortisol.
- Absence of food increased anxiety behavior, but not cortisol levels.

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ABSTRACT

The effect of a high (chocolate) versus low fat/sugar (chow) food on a conditioned-place-preference (CPP) task was evaluated in marmoset monkeys. Anxiety-related behaviors and cortisol levels before and after the CPP task were also measured. Subjects were habituated to a two-compartment CPP box and then, on alternate days, had access to only one compartment during daily 15-min conditionings, for a total of 14 trials. Marmosets were provisioned with chocolate chips in the CC-paired compartment on odd-numbered trials and standard chow in the CW-paired compartment on even-numbered trials. They were then tested for preferring the CC-paired context after a 24-h interval. During the conditioning, a significantly greater amount (in kcal/trial) of chocolate was consumed than chow, yet the foraging pattern of both food types was similar. On the test trial, the time spent in the CC-paired context increased significantly compared to pre-CPP levels, yet this response was not readily predicted by baseline behavioral or cortisol levels. Also, the chocolate CPP response was positively correlated with foraging time, rather than the amount of calories consumed. The sudden absence of the food increased exploration, while the chocolate CPP effect was associated with vigilance — both anxiety-related behaviors in marmosets. This behavioral profile occurred regardless of any concomitant change or correlation with cortisol. Therefore, the high fat/sugar food was more prone to be overly consumed by the marmosets, to induce a CPP response and to lead to anxiety-related behavior in its absence.

1. Introduction

The control of ingestive behavior is exerted by a complex interaction between homeostatic (or allostasis) gut-brain mechanisms and reward-associated circuits [1–3]. Food is actually a natural rewarding stimulus, having both hedonic ('liking') and motivational ('wanting') elements [2]. However, primary physiological homeostatic circuits may be entirely overridden by the brain's reward system, particularly when it becomes overactivated by an excessive consumption of highly palatable foods [1,4]. Such a biased control contributes, among other aspects, to the development of food-addiction-related behaviors via mechanisms that are decidedly similar to that of more putative rewards (i.e., drugs; reviewed in [5]). Foods with high levels of fat, sugar, salt and/or artificial flavors and additives are perceived as 'hyperpalatable' and are potentially more prone to induce a food-addiction state than traditional/wholesome items (i.e., fresh fruits and vegetables; [6]), particularly under specific restricted feeding schedules [7].

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In rodents, hyperpalatable foods are reported to induce self-administration [8], compulsive binge-type behavior [9], environmentally-triggered conditioned responses [10], behavioral signs of withdrawal [11], re-instatement of extinguished responding [10,12], cross-sensitization with drugs of abuse [13] and persistent food-seeking despite negative consequences [14,15]. They also trigger long-lasting neuroadaptive responses in dopamine signaling within the brain's reward system [14,16]. On the other hand, less-palatable items (e.g., regular diet/chow) seem to have lower hedonic properties, are not usually overly-consumed, can be regulated effectively by typical homeostatic signaling and have a minor long-term impact on mesolimbic dopamine neurotransmission [14,17,18].

Be that as it may, only few studies have focused on the rewarding properties of food using nonhuman primates (NHP) [19–22]. They are highly suitable subjects for a more translational approach to humans considering that, within the reward system, dopamine differs between rodents and NHPs, particularly in terms of connectivity and prenatal development [23–25], release and uptake [26], genetic homology of the sinaptosomal transporter [27] and receptor density/distribution [28]. Recently, both food [19,21,22] and addictive drugs [29,30] were found to induce a conditioned-place-preference (CPP) in NHPs. This effect is based on an associatively-learned preference for certain locations that is acquired in response to experiencing a rewarding agent at that same location [31,32]. Chocolate was recently found to induce a lasting CPP memory in marmosets [19], but control animals were not exposed to any food item. Thus, the effect of high versus low fat/sugar (palatable) foods have yet to be determined in NHPs. Here we evaluated whether marmoset monkeys acquire a conditioned preference for the location where they consumed a high (chocolate) versus less-palatable food (chow). Chocolate was used, as in humans it has an elevated hedonic rating [33,34] and prominent craving-inducing property [35], while in animals it activates reward circuits when voluntarily consumed [15, 36,37]. Behavioral indicators of anxiety and cortisol levels were also measured before and after the CPP task. Stress is an important factor that regulates food intake and contributes to addiction-like behaviors [38].

2. Materials and methods

2.1. Subjects and housing conditions

Six adult captive black tufted-ear marmosets (*Callithrix penicillata*; 3 males, 3 females) were used, weighing 290–390 g at the beginning of the study. They were housed in pairs, within separate home-cages, at the Primate Center of the University of Brasilia in cages (2 × 1 × 2 m each) of a same colony room. This room consisted of a semi-outdoor/indoor housing system with two parallel rows of 12 cages each, separated by a common wire-mesh enclosed central corridor. The animals were thus exposed to natural light, temperature and humidity conditions. Fresh food was provided at 07:00 h and removed 17:00 h, consisting of a mixture of pieces of fruits and vegetables. Boiled eggs, nuts and/or cooked chicken breast were given several times a week. Water and dry food pellets (chow) were available ad libitum. The same chow also served as the less-palatable food (see Behavioral procedure and analyses below). Animals were not food or water deprived, except during specific trials also indicated in the procedure below. For further housing conditions see [21]. These complied with the regulations of the Brazilian Institute of Environment and Renewable Natural Resources (IBAMA).

2.2. Apparatus and experimental set-up

Testing was conducted in a two-compartment CPP box, suspended 1 m from the floor. For each compartment (60 × 60 × 35 cm), three walls and the floor were made of aluminum, whereas glass was used for the fourth wall and the top. However, each compartment had different visual and tactile cues: one was white with a smooth surface, whereas the other had black and white diagonal stripes with a rough surface. The aluminum wall that divided the CPP box into two compartments consisted of a horizontally-sliding door. If retracted, it gave subjects direct access to both sides of the apparatus. Each compartment, however, had an independent entry/exit point consisting of a horizontally-sliding door located on the aluminum side directly opposite the glass wall. Attached to the apparatus, and encompassing both access doors, was a common aluminum antechamber (15 × 10 × 35 cm). Subjects could only access the compartments' sliding doors and enter the respective compartment via this common antechamber, which in turn had a guillotine-type door as its access point. In addition, a stainless-steel bowl (9 cm diameter, 5 cm height) was placed on a metal support fixed to the floor of each compartment and thus could not be displaced by the marmosets. Each bowl was located in the corner opposite to the compartment's access point. These bowls were used for placing food rewards on specific trials (see Behavioral procedure and analyses below).

The CPP box was set-up in a test-room 50 m away from the colony facility. Subjects were transported between their home-cages and the test-room via a transport-cage (35 × 20 × 23 cm). This aluminum box prevented them from seeing their surrounding and attached directly to the guillotine-type door of the CPP box's antechamber. The apparatus was monitored via a closed-circuit system using two digital cameras (Fire-i, Unibrain, USA): one was mounted 1.5 m above the CPP box and the other was set 1.5 m in front of its glass wall. These provided a top- and side-view, respectively. Both cameras were connected to a laptop, placed in an observation-room adjacent to the test-room, on which all tracking and behavioral recordings took place.

2.3. Behavioral procedure and analyses

Marmosets were submitted to a CPP protocol similar to that used in previous studies in this NHP [19,21,39]. Each marmoset was initially submitted to a daily 15-min habituation trial in the CPP box on three consecutive days. On these three trials, food was not provided in either compartment and the common sliding-wall was kept partially retracted, thus providing a direct 20-cm passage between compartments. As a general innate preference for either context was not observed, an unbiased apparatus design was used during the subsequent phases.

The marmosets were then submitted to a daily 15-min conditioning trial in the CPP box during 14 consecutive days. On these trials the common sliding-wall remained shut at all times with no direct connection between the two compartments. Accordingly, on alternate days, each marmoset was given access to either the white or striped compartment. On odd-numbered trials (i.e., days 1, 3, 5, 7, 9, 11 and 13) 50 g of chocolate chips were provided in the food bowl of the open compartment — chocolate-chip paired context (CC-paired). On even-numbered trials (i.e., days 2, 4, 6, 8, 10, 12 and 14), 50 g of regular chow were provided in the food bowl of the opposite compartment — chow-paired context (CW-paired). Half of the subjects were arbitrarily conditioned to chocolate in the white context and chow in the striped compartment, while the other half was chocolate/chow conditioned in the opposite context. The chocolate chips contained 5.32 kcal/g: 0.64 g carbohydrate, 0.29 g fat, 0.04 g protein, and 0.03 g fiber (Chipshow milk chocolate, Harald, São Paulo, Brazil) and chow had 3.87 kcal/g: 0.0 g carbohydrate, 0.09 g fat, 0.31 g protein, and 0.04 g fiber (Purina cat chow, Nestlé, Ribeirão Preto, Brazil). Also, the regular daily diet was removed from the subjects' home-cages 2 to 4-h prior to each session.

To determine if a place-preference response was acquired, all subjects were subsequently submitted to a single 15-min test trial in the CPP box, 24-h after the last conditioning. During this trial, each marmoset could once again simultaneously access both compartments, as the common sliding-wall was kept partially retracted. Food was not provided in either context during the test trial.