Physiology & Behavior 157 (2016) 13–19

Contents lists available at ScienceDirect

Physiology & Behavior

journal homepage: www.elsevier.com/locate/phb

Differential motivational profiles following adolescent sucrose access in male and female rats

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HIGHLIGHTS

- Male and female rats were exposed to intermittent sucrose across adolescence.
- Motivation was assessed by lever pressing on a progressive ratio schedule.
- Female rats exposed to sucrose were more motivated to procure sucrose as adults.
- Male rats exposed to sucrose were less motivated to procure sucrose as adults.
- Intermittent sucrose access during adolescence has sex-dependent motivation effects.

ARTICLE INFO

Article history:
Received 13 September 2015
Received in revised form 24 January 2016
Accepted 26 January 2016
Available online 27 January 2016

Keywords:
Dopamine
Binge eating
Progressive ratio
Sex differences
Motivation
Adolescence

ABSTRACT

Adolescents are the highest consumers of sugar sweetened drinks. Excessive consumption of such drinks is a likely contributor to the development of obesity and may be associated with enduring changes in the systems involved in reward and motivation. We examined the impact of daily sucrose consumption in young male and female rats ($N = 12$ per group) across the adolescent period on the motivation to perform instrumental responses to gain food rewards as adults. Rats were or were not exposed to a sucrose solution for 2 h each day for 28 days across adolescence [postnatal days (P) 28–56]. They were then trained as adults (P70 onward) to lever press for a palatable 15% cherry flavored sucrose reward and tested on a progressive ratio (PR) schedule to assess motivation to respond for reinforcement. Female rats exposed to sucrose had higher breakpoints on the PR schedule than controls, whereas male rats exposed to sucrose had lower breakpoints than controls. These results show that consumption of sucrose during adolescence produced sex-specific behavioral changes in responding for sucrose as adults.

1. Introduction

Excessive consumption of high sugar foods and drinks is thought to play a central role in the development of obesity in humans. Increasing sugar consumption affects the majority of the developed and developing world [1, 2] and soft drinks are the largest single source of added sugar consumed today [3]. The physical health consequences of sugar overconsumption such as weight gain and cardiovascular disease are well documented [3]. However, less is known about how sugar consumption affects learning and motivational processes.

People select sugar rich foods for consumption because they are readily available and provide a relative cheap source of calories. However, high sugar foods are also highly palatable and people come to crave them in a manner analogous to the cravings for psychoactive drugs, a form of food addiction. The concept of food addiction has been postulated as a causal factor in phenomena such as chronic overeating, binge eating, and obesity [4]. More recently, it has been proposed that binge eating could be a behavioral addiction, as opposed to a substance directed food addiction [5]. In population studies, females are more likely to suffer from eating disorders, including anorexia and bulimia nervosa, than males [6]. Nevertheless, males comprise a substantial proportion of binge eating disorder cases [7, 8], and binge eating is prevalent among adolescents and young adults of both genders [9]. The psychological characteristics associated with binge eating include negative emotions, such as depression, anger and frustration [10], and female binge eaters are more prone to eat as a coping response to negative affective states than males [11]. Due to the uncontrolled nature of binge eating episodes, it has been viewed as an addiction-

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http://dx.doi.org/10.1016/j.physbeh.2016.01.038
0031-9384/

like behavior [12]; a view supported by the finding that adolescents who are binge eaters are also more likely to use addictive substances [13].

Animal models have shown that access to palatable foods such as sucrose for a limited period each day across a number of days activates the mesocorticolimbic dopamine system in a manner analogous to drugs of abuse [14]. These models have also shown sex-differences in responses to drugs of abuse. For example, female rodents have an increased sensitivity to psychomotor stimulating effects of methamphetamine [15, 16] and increased motivation to self-administer psychostimulants [17]. Given the potentially addictive nature of high sugar diets, females could also be more vulnerable to the effects of such diets. Moreover, because adolescent sugar intake in people is higher than any other age group, female adolescents may be more vulnerable to the long-term effects of sugar intake than adolescent males [18, 19]. Thus, we sought to determine the effects of daily sugar consumption in adolescent female and male rats on their performance as adults in a task which assessed their motivation to respond for food reward. In rats, adolescence includes the pubertal period and extends from postnatal day (P) 28–42, although developmental alterations in the prefrontal cortex may extend to P55 [20].

The task used was a progressive ratio (PR) schedule. In this schedule, the number of responses required to procure a reward, such as food (or drug), is progressively increased in order to assess how many responses the animal is prepared to make for the reward; essentially, the cost is progressively increased. The "breakpoint" is the maximal number of responses an animal is prepared to make to procure the reward, and is used as a measure of the incentive value of the reward [21, 22]. Previous studies have shown that male rats who had over-consumed sugar as adolescents, but not as adults, were less motivated to respond for rewarding solutions as adults, indicated by lower breakpoints than control rats [23]. We sought to replicate the effect of adolescent sucrose intake in male rats on their motivation as adults and further assess whether sucrose intake in adolescent females also altered motivation as adults. We provided sucrose to male and female rats across their adolescence and trained them as adults to perform lever press responses for a reward. Finally, we tested their breakpoints in the PR schedule responding relative to male and female rats not exposed to sucrose across their adolescence.

2. Materials and methods

2.1. Subjects

Male ($N = 24$) and female ($N = 24$) albino Sprague Dawley rats (Animal Resources Centre, Western Australia) arrived in the laboratory at 3 weeks of age (mean weight males: 80 g, females: 72 g). They were housed in plastic cages ($26 \times 40 \times 60$ cm) with 4 rats per cage in a colony room with a 12 h light-dark cycle (lights on at 07:00 h), maintained at a temperature of 21 ± 2 °C and a humidity of $55 \pm 5\%$. Rats were acclimated to the laboratory for 7 days during which they were handled each day. Rats were weighed once per week at 08:00 h prior to sucrose access (in sucrose exposed rats). Training and testing occurred in the light phase between 09:00 and 17:00 h. The experimental procedures were approved by the University of New South Wales Animal Ethics Committee in accordance with the Animal Code of Practice for the Care and Use of Animals for Scientific Purposes.

2.2. Sucrose access

After the 7 days of acclimating (P21–P27), rats in the sucrose access condition (males $N = 12$, females $N = 12$) were permitted 2 h access to 200 ml of 10% sucrose (w/vol; CSR® white sugar; Victoria, Australia) between 08:00 and 10:00 h every day for 28 days (P28–P56) (see Fig. 1a for timeline of experimental events). Two bottles containing sucrose were provided to each of the three cages containing the males and the three containing the females. The sucrose solution provided a caloric density (1.7 kJ/ml), similar to that of commonly available sugar-sweetened beverages. Consumption was recorded by weighing the bottles before and after the 2 h sucrose access period and the volume consumed by the four rats in each cage was calculated. All rats had *ad lib* access to chow and water at all times. From P60 rats were maintained on a fluid deprivation schedule which consisted of providing water for 3 h per day 30 min after experimental sessions from 13:00 to 16:00 h. Behavioral training began at P70. Chow continued to be available *ad libitum*.

2.3. Behavioral procedures

2.3.1. Instrumental training

Instrumental training took place in eight chambers (Med Associates, St Albans, VT), each measuring 30 cm wide, 21 cm high and 24 cm deep, located in sound-attenuating boxes (Med Associates). The ceiling, door and back wall of each chamber were clear Perspex and the left and right walls were stainless steel. The floor of each chamber was constructed of 19 stainless steel rods (4.8 mm in diameter, spaced 16 mm apart). The right hand side wall of the chambers contained a recessed magazine where palatable sucrose reinforcement (0.3 ml, 15% w/v flavored with 0.05% cherry Kool Aid), was delivered by a dipper. Cherry flavour was added to the 15% sucrose to make the reinforcer novel to both control and sucrose-exposed rats. Two retractable levers were located to the left and right of the magazine. Entries to the magazine were detected by an infra-red sensor. A 3 W house light was located at the top centre of the left wall. A computer equipped with MED-PC software (version IV; Med Associates Inc.) controlled the experimental events and recorded data.

Rats were familiarized with the conditioning chambers and with the delivery of sucrose into the magazine for 2 sessions. Rats were trained to press one of the two levers (the active lever) on a continuous reinforcement schedule for one session and then a variable-ratio (VR) 2 schedule (on average every 2 responses resulted in sucrose delivery) for the remaining sessions. Session duration was 40 min. Presses on the other lever (inactive lever) had no programmed consequences. The positions of the active and inactive levers were counterbalanced across rats in each of the groups.

2.3.2. Progressive ratio

Following training under the VR2 schedule, rats received a test session under a PR schedule. The PR schedule was based on the following exponential progression: 1, 2, 3, 4, 6, 8, 10, 13, 16, 20, 25, 31…, derived from the formula $[0.5 * ((5 \times e0.2n) - 5)]$, rounded to the nearest integer, where n is the position in the sequence of ratios (Roberts & Richardson, 1992). For each reinforced response, the animal received 0.3 ml of cherry flavored sucrose (15%). The breakpoint was defined as the last

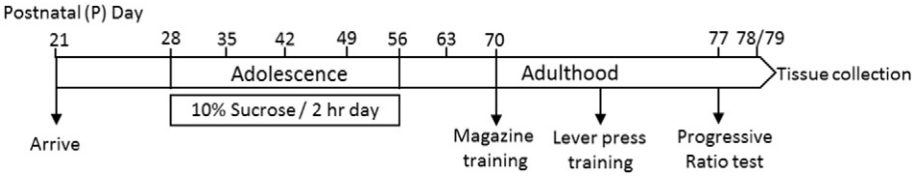

Fig. 1. Timeline of experimental events.