ELSEVIER

Physiology & Behavior 91 (2007) 424–431

PHYSIOLOGY & BEHAVIOR

Body composition and endocrine status of long-term stress-induced binge-eating rats

A.I. Artiga, J.B. Viana, C.R. Maldonado, P.C. Chandler-Laney, K.D. Oswald, M.M. Boggiano *,[1]

Department of Psychology, Behavioral Neuroscience Division, University of Alabama at Birmingham, Birmingham, AL 35294-1170, USA

Abstract

Clinical binge eating runs a protracted course. The etiology of binge eating remains perplexing in part because, in humans, it is difficult to isolate and assess the independent and aggregate impact of various contributing variables. Using rats, we found that footshock stress and a history of caloric restriction (S+R), combine synergistically to induce binge eating. Stress and dieting are also strong antecedents and relapse factors in human eating disorders. Here we report further behavioral and physiological parallels to human binge eating. Like the protracted course of human binge eating, young female Sprague–Dawley rats continued to binge eat after 23 restriction/stress cycles (7 months) and this despite experiencing no significant weight loss during the restriction phases. Stress alone reduced adiposity by 35% ($p<0.001$) but S+R rats had no significant fat loss. An endocrine profile of normal plasma leptin and insulin levels but marked elevation of plasma corticosterone levels was found only in the binge-eating (S+R) rats ($p<0.01$), also paralleling endocrine profiles reported in clinical binge-eating studies. These behavioral and physiological similarities between this animal model and clinical binge eating increase its utility in understanding binge eating. Importantly, our findings also highlight the stubborn nature of binge eating: once a critical experience with dieting and stress is experienced, little if any further weight loss or food restriction is necessary to sustain it.

Keywords: Corticosterone; Caloric restriction; Hyperphagia; Weight cycling; Dieting; Leptin; Insulin; Food restriction; Bulimia; Overeating; Palatable food; Body fat; Lean mass; Animal model

Binge eating is a central feature of eating disorders, including many cases of anorexia nervosa, and, by definition, all cases of bulimia nervosa and binge-eating disorder (BED) [1]. The course of bulimia nervosa is long, typically ten years, and for BED, it can be a lifetime [1]). Binge eating is also estimated to characterize a large percentage of the obese population, and in this population, binge eating contributes to their obese state [2].

In the clinical literature several variables have been identified as possible "triggers" for binge eating, including dieting, stress, and negative affect [1,12,14]. Although a history of dieting is a common antecedent of binge eating, bingeing can persist despite a cessation of dieting or only occasional dieting. In fact, hunger is a weak trigger of binge eating compared to negative affect and stress [3–7]. Indeed, in individuals with bulimia, hunger can even increase after a meal [8], and a diagnostic feature of BED is eating large amounts of food when not hungry [1]. It is clear that binge eating occurs in the absence of negative energy balance. Furthermore, most individuals with bulimia are normal weight and, as mentioned previously, those with BED are often overweight [1].

Preclinical models of binge eating offer a means of directly testing cause–effect relationships by environmental variables and a window into the physiological underpinnings of this highly recidivistic disorder. The binge-eating rat model described here was developed in our laboratory. Only those rats with a history of cyclic caloric-restriction binge when stressed with footshock [9,10]. This simulates the proclivity for stress-induced hyperphagia, versus hypophagia, in dieters [11], and is consistent with dieting and stress as key etiological features in eating disorders [12–14]. A minimum of three

* Corresponding author. 415 Campbell Hall, 1300 University Blvd. University of Alabama at Birmingham, Birmingham, AL 35294-1170, USA. Tel.: +1 205 934 2439; fax: +1 205 975 6110.

E-mail address: boggiano@uab.edu (M.M. Boggiano).

[1] Formerly M.M. Hagan.

0031-9384/$ - see front matter © 2007 Elsevier Inc. All rights reserved.
doi:10.1016/j.physbeh.2007.04.001

restriction–refeeding cycles is needed to evoke binge eating in the binge-eating rats [9,10]. Unlike the limited amount of time with palatable food (PF) that is integral in some models to produce binge eating [15,16], we allow them an unrestricted time with PF. Also of clinical relevance, since many individuals with eating disorders, namely bulimia nervosa and BED, do not experience drastic weight loss, our model does not rely on dramatic levels of caloric restriction or drastic fluctuations in body weight for binge eating to be sustained.

Here we further explore: 1) whether binge eating in this model is sustained after a long history of restriction and stress; 2) whether once binge eating is established, it persists despite minimal if any caloric restriction-induced weight loss; achieved with shorter cycles, and 3) whether a history of restriction and stress imposes unique changes in body composition and/or endocrine parameters. We also describe the body composition and hormonal status of the binge-eating rats with particular attention to hormones involved in the regulation of feeding and stress.

While the effect of acute total food deprivation and of environmental stressors on circulating levels of leptin, insulin, and corticosterone (CORT) has been studied in rats, little is known regarding the effect of a prolonged human-like history of dieting, alone, or coupled with stress, on these parameters. This is information that will be useful in interpreting changes in brain and behavior found with this animal model and in applying this information to better treat binge eating. Knowledge of the status of endocrine hormones known to interact with these brain substrates of feeding, reward, and mood is needed for a more complete understanding of the physiology of binge eating, and may raise clues as to the motivation behind the rats' binge eating.

Traditionally, our stress-restriction protocol used long (12 day) cycles of restriction and refeeding. Rats in the restricted groups lost up to 10% of their body weight during the restriction phase then were allowed to recover their weight prior to being stressed for the feeding test [9,10]. Here, once binge eating on palatable food was observed (at the end of the 4th restriction–refeeding cycle), the rats were switched to short cycles. Hence, the 5th cycle was the first short cycle. We also repeated these cycles for a total of 23 cycles to assess the duration and robustness of their binge eating after this protracted time (7 months) with dieting and stress. Finally, we obtained measures of lean tissue, fat, and bone mass and determined plasma levels of leptin, insulin, glucose, and CORT in control rats, rats with restriction-history only, with stress only, and with the combined restriction-history and stress that results in binge eating.

1. Methods

1.1. Subjects

A total of $N=25$, 70-day-old female Sprague–Dawley rats were acclimated to individual cages with ad lib chow and water in individual bedded cages under a 12:12 light/dark cycle (lights off at 1200). The rats were weight-matched and assigned to one of four groups ($N=6/7$ per group): a no history of restriction/no-stress group (Control); a no history of restriction/stress group (Stress); a history of restriction/no-stress group (Restrict); and the binge-eating group, the history of restriction/stress group (S+R). The University of Alabama at Birmingham Institutional Animal Care and Use Committee approved all of the experimental procedures.

1.2. Diets

Diets used included regular rat chow and Nabisco Double-Stuf Oreo cookies. Oreo cookies served as the highly palatable food (PF) and are composed of 43% kcals from fat, 57% kcals from carbohydrate, trace protein (0.02% kcals), and contain 4.83 kcals/g (Nabisco, Hanover, NJ). Regular rat chow (Harlan-Teklad, Indianapolis, IN) is composed of 3.5% kcals from fat, 70% kcals from carbohydrate, 17% kcals from protein, 10% moisture, and contains 3.74 kcals/g.

1.3. Cyclic caloric restriction–refeeding and stress protocol

For the first four cycles of the study the cyclic restriction–refeeding/stress procedure was followed as previously described [9,10]. Table 1 details the protocol and for the first 3 cycles, the "long cycles" were used. Briefly, during the restriction phase, rats in the Restrict and S+R groups received 5 days of a restricted amount of chow (66% of the Control's daily chow intake prior to the start of cycling); while the Control and Stress groups received ad lib chow. On the 6th and 7th days, to simulate

Table 1
Cyclic restriction–refeeding and stress protocol for binge-eating including use of long and short restriction–refeeding phases

Phase of Cycle:	Restriction	Refeeding with PF	Refeeding without PF	Test Day
Long Cycle →	Day 1-5	Day 6-7	Day 8-11	Day 12
Short Cycle* →	Day 1-3*	Day 4*	Day 5-6*	Day 7*
GROUPS ↓				
Control	Ad lib chow	Ad lib chow+PF	Ad lib chow	No stress
Stress Only	Ad lib chow	Ad lib chow+PF	Ad lib chow	Stress
Restriction Only	66% of chow *50% of chow	Ad lib chow+PF	Ad lib chow	No stress
Stress+Restriction	66% of chow *50% of chow	Ad lib chow+PF	Ad lib chow	Stress

The long (traditional) cycles were used in cycles 1-4, and the short cycles* were used in cycles 5-23.
PF=palatable food (cookies); 66% and 50% of chow was determined from control groups' mean 24 hr intake over 3 days prior to onset of the first cycle.