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Consummatory, anxiety-related and metabolic adaptations in female rats with alternating access to preferred food

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Summary Avoidance of and relapse to palatable foods is a qualitative aspect of dieting, a putative risk factor for eating disorders or obesity. The present studies tested the hypotheses that rats with alternating access to highly preferred foods would show: (1) hypophagia, a function of the relative hedonic value of the underaccepted diet, (2) increased anxiety-like behavior and psychomotor arousal when preferred diet was unavailable, (3) obesity-like changes, and (4) stable individual differences in diet-switch-induced hypophagia. Preferences among three high-carbohydrate diets were determined in female Wistar rats ($n = 16$). Adolescent rats ($n = 162$) received the following weekly diet schedules: (1) continuous regular chow (7 days/week), (2) chow (5 days/week) followed by a *more* preferred diet (2 days/week), or (3) chow (5 days/week) followed by a *less* preferred chow (2 days/week). Some animals were yoke-restricted (75% calories) when provided chow to increase its rewarding properties. Diurnal locomotor activity was measured in a familiar environment, and anxiety-like behavior was assessed in the elevated plus-maze and defensive withdrawal tests. Rats withdrawn from the preferred diet showed hypophagia, anxiogenic-like behavior, increased locomotion, and weight loss. Chow hypophagia was progressive, individual-specific in magnitude, (partly) non-homeostatic in nature, and blunted by previous chow restriction. Despite eating less, rats cycled with the preferred diet became heavier, fatter, and diurnally less active, with greater feed efficiency and proinflammatory

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adipokine levels than chow controls. The present diet cycling procedure may model consummatory, anxiety-related, and metabolic effects of qualitative dieting in humans.

1. Introduction

Access to tasty, calorie-rich foods, promotes overeating (Yach et al., 2006). Paradoxically, individuals who restrict the types or quantities of foods that they eat putatively are at greater risk for eating disorders or obesity, although data in this regard are mixed (Polivy and Herman, 1985; Stice et al., 2005). Restrained eaters often limit themselves to "safe" foods, typically less palatable than energy-dense "forbidden" foods (Gonzalez and Vitousek, 2004; Stirling and Yeomans, 2004), to which they often return. Avoiding "forbidden" foods may thereby incidentally, but systematically, vary food palatability across time, experiences that might alter the control of feeding.

Indeed, when animals are switched from preferred to less preferred diets, exaggerated reductions in food intake occur (Archer et al., 2005; Corwin, 2004). Time-limiting access to palatable foods also alters the short-term control of feeding; restricted daily access ($\leq$2 h/day) leads to binge-like intake of preferred food and reduced intake of less preferred foods between palatable food access (Bello and Hajnal, 2006; Corwin, 2006; Cottone et al., 2008). Yet, the effects of repeated, sustained alternations in food palatability, a schedule more like what occurs when humans avoid and relapse to "forbidden" foods, on the control of daily food intake are less known.

In this context, Boggiano (formerly Hagan) and colleagues developed a binge eating model that involves cycles of 2-day dietary supplementation with high-fat, palatable cookies, separated by multiple days of chow access only. In this model, rats with a joint history of caloric restriction during chow access followed by refeeding with cookies show increased intake of palatable food after footshock (Hagan et al., 2002). The control group in this model is *ad libitum*-fed rats that receive intermittent, supplementary access to cookies (Boggiano et al., 2007). However, research with children suggests that intermittent access to palatable foods itself may alter the acceptance (1-choice intake) and preferredness (multiple-choice relative intake) of foods (Birch and Davidson, 2001; Fisher and Birch, 1999). Consistent with this possibility, control subjects in the binge model show long-lasting reductions in deprivation-induced chow intake compared with rats that never tasted cookies (Hagan and Moss, 1997). The present studies therefore sought to test explicitly the hypothesis that short-term food intake by rats receiving alternating access to differently preferred high-carbohydrate foods becomes more controlled by relative diet palatability over cycles of access. This was predicted to be seen as increasing hyperphagia of the preferred food and increasing hypophagia of the otherwise acceptable, but less preferred, diet compared with chow-fed controls.

Intermittent access to rewarding drugs of abuse leads to negative emotional states when the rewarding substance is no longer available, perhaps due to allostatic, opponent-process shifts in brain reward circuitry (Koob and Le Moal, 2001; Solomon and Corbit, 1974). Such negative emotional states putatively motivate substance use via negative reinforcement mechanisms. Perhaps analogously, negative mood, anxiety, and tension are associated with intermittent dieting (Laessle et al., 1989) or switching to a low-fat diet (Wells et al., 1998) in humans and are suspected triggers of overeating palatable food (Hagan et al., 2002; Waters et al., 2001). Moreover, cessation of exposure to ethanol (Taylor et al., 2006) or opiates (Stinus et al., 1998), as well as stressors (Sabino et al., 2005), also is known to increase sleep-phase locomotor activity in familiar environments. Thus, the present study also tested the hypothesis that rats with alternating access to highly preferred foods would show increased anxiety-like behavior and psychomotor arousal when preferred diet was unavailable.

Voluntarily (Polivy and Herman, 1985; Stice et al., 2005) or involuntarily (Birch and Davidson, 2001) receiving intermittent access to palatable food has been proposed to promote obesity. However, an alternative explanation is that the behavior of restricting access to palatable food is a risk *marker* for individuals who otherwise would overeat or gain weight (Lowe and Kral, 2006). Thus, the present study tested the hypothesis that rats with alternating access to highly preferred foods would show obesity-like changes.

Finally, previous studies have reported individual differences in the propensity to overeat palatable food in a binge-like manner (Boggiano et al., 2007; Cottone et al., 2008) and conversely, in the magnitude of undereating an alternative tastant after prior access to a more palatable (Freet et al., 2006) and/or energy-dense food option (Levin and Dunn-Meynell, 2002). Thus, the present study tested the hypothesis that rats showed stable individual differences in the propensity to undereat chow after prior access to a more preferred food of similar energy density and macronutrient proportions.

In summary, the present studies tested the independent hypotheses that rats with alternating access to highly preferred foods would show: (1) progressively greater hypophagia of the less preferred diet, (2) increased anxiety-like behavior and psychomotor arousal when preferred diet was unavailable, (3) obesity-like changes, and (4) stable individual differences in diet-switch-induced hypophagia. To test the role of non-nutritional (e.g., hedonic) factors in food intake adaptations, as opposed to increased adiposity or other energy homeostatic factors, several procedures were used. First, diets were chosen to differ in preferredness, and less so in energy density or macronutrient proportions. Second, relationships between undereating of chow on the one hand and body weight and adiposity on the other were examined. Third, some animals were offered alternating access to a *less* preferred diet that would not promote weight gain. Finally, the reward associated with chow diet was increased by calorically restricting rats during chow access. This experiment followed from the premise that if hypophagia of chow was due to a negative hedonic comparison of the chow to the preferred food, then increasing the rewarding properties of chow via concurrent food restriction should reduce underacceptance of chow selectively in the diet-cycled group. Conversely, if food restriction was