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Social Status Predicts Response to Dietary Cycling In Female Rhesus Monkeys

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Abstract

With the prevalence of obesity among women the United States surpassing 40%, it is critical to understand how environmental factors influence appetite, body fat accumulation, and the ability to lose weight and maintain weight loss. Psychosocial stress exposure is a risk factor for increased consumption of calorically dense diets (CDD), which are high in fat and sugars and promote both increased food intake and weight gain. However, it remains unclear how appetite is affected by psychosocial factors when people striving to lose weight restrict intake of unhealthy, calorically dense foods. Using a translational non-human primate model of chronic psychosocial stressor exposure in females (n=16), mediated by social subordination, we examined *ad libitum* food intake, weight change, and social behavior during three consecutive, 15-week dietary conditions: 1) obesogenic, dietary choice; 2) chow-only; and 3) a switch back to dietary choice. Data showed that a choice dietary environment that includes both chow and CDD promotes increased calorie consumption of CDD in subordinate female rhesus monkeys during the baseline choice and back-to-choice phases (p=0.016). Removal of the CDD during the chow-only phase resulted in mild inappetence (p=0.005) and a loss in body weight (p<0.001) in subordinate females. Reintroduction of the CDD to subordinate, but not dominant, females was associated with increased calorie intake that surpassed baseline intake (p<0.001), and greater body weight gain (p=0.026). There were no effects of diet cycling on total food intake and body weight change in dominant females (p's>0.05). Overall, our results suggest that adverse psychosocial experience is associated with increased preference for highly palatable, calorically dense food in a choice dietary environment.

Keywords

social status; psychosocial stress; diet cycling; food intake; body weight; female monkeys

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1. INTRODUCTION

Diet-related chronic diseases represent the single largest cause of morbidity and mortality in Western societies (Cordain, et al., 2005). These diseases arise from excessive consumption of calorically dense diets (CDD), comprised of foods such as dairy products, refined sugars, saturated fats, and salts (Cordain, et al., 2005). Resulting obesity has a prevalence rate of 40.4% among women the United States (Flegal, Kruszon-Moran, Carroll, Fryar, & Ogden, 2016). Not surprisingly, individuals with obesity often fail to lose weight (Ochner, Barrios, Lee, & Pi-Sunyer, 2013) and even when they are successful, only 54% of weight loss is maintained one year after a lifestyle intervention that involves both dietary and physical activity components (Barte, et al., 2010). As solutions are sought for the obesity epidemic, it is critical to understand how environmental factors influence appetite.

Consumption of an obesogenic diet that is high in fat and processed sugars compromises reward pathways and promotes food intake and weight gain (Johnson & Kenny, 2010; Morin, et al., 2017). Studies in people (Annesi, 2016; Epel, Lapidus, McEwen, & Brownell, 2001) and animals (Dallman, et al., 2006; Michopoulos, Toufexis, & Wilson, 2012) show that an obesogenic dietary environment interacts with chronic stressor exposure to further increase eating. Indeed, chronic stressor exposure is a contributing factor for obesity (Razzoli, Pearson, Crow, & Bartolomucci, 2017). By mediating the release of glucocorticoids, chronic stressor exposure alters food salience and increases caloric intake of palatable CDD (Warne, 2009). Additionally, signals from the stress axis target corticostriatal-limbic reward circuits (Harfstrand, et al., 1986; Sauvage & Steckler, 2001; Swanson, Sawchenko, Rivier, & Vale, 1983) and increase the risk for developing an addictive phenotype (Anisman & Matheson, 2005; G. Koob & Kreek, 2007; G. F. Koob & Le Moal, 2001), likely further compromising diet-induced changes in reward circuits. This observation that chronic stressor exposure increases food intake contrasts with reports that stressor exposure produces inappetence and weight loss in animal models fed a low calorie, chow diet (Smagin, Howell, Redmann, Ryan, & Harris, 1999). The apparent discrepancy between findings can be attributed to the exogenously manipulated dietary environment: under conditions of chronic stress, dietary choice of CDD promotes hyperphagia whereas dietary restriction to chow produces hypophagia.

Despite these findings, it remains unclear how appetite is affected by psychosocial factors when people striving to lose weight change their dietary environment to restrict intake of CDD. Rodent studies indicate that alternating availability of chow and preferred, CDD progressively produces hypophagia during chow-only diet phases but promotes binge-like overeating during preferred diet phases (Blasio, Rice, Sabino, & Cottone, 2014; Carlin, et al., 2016; Eikelboom & Hewitt, 2016; Martire, Westbrook, & Morris, 2015). Similarly, human studies indicate that weight cycling, reflecting periods of dietary restriction followed by unrestrained eating, increases the probability of subsequent weight gain (Mackie, Samocha-Bonet, & Tam, 2017). While informative, these studies do not consider the impact of stressor exposure on appetite in a changing dietary environment.

Our group has leveraged a well-characterized, translational model in female rhesus monkeys that produces a number of stress-related phenotypes (Michopoulos, Higgins, Toufexis, &

Wilson, 2012; Snyder-Mackler, et al., 2016) to examine the interaction between chronic stress and appetite. Our previous research has shown that social subordination in female monkeys results in significantly greater caloric intake when monkeys are provided three-week *ad libitum* access to an obesogenic dietary environment that includes a choice between a low calorie laboratory chow diet (“chow”) and CDD (Michopoulos, Toufexis, et al., 2012). In the current study, we examined food intake, weight change, and social behavior during three consecutive, 15-week dietary conditions: 1) obesogenic, dietary choice; 2) chow-only; and 3) a switch back to choice. We hypothesized that subordinate females experiencing chronic psychosocial stress would consume more calories and gain more weight than dominant females during the choice dietary conditions. In contrast, we predicted that the subordinate females would consume fewer calories and lose more weight than dominant monkeys during the chow-only phase. This study leverages a translational non-human primate model of chronic psychosocial stressor exposure to advance our understanding of the relationship between adverse psychosocial experience and ingestive behavior in a dynamic, exogenously manipulated dietary environment.

2. MATERIALS AND METHODS

2.1 Animals

Subjects were adult female rhesus monkeys ($n=16$; 13.5 ± 0.5 years) living in indoor-outdoor enclosures at the Yerkes National Primate Research Center Field Station. The subjects lived in one of three small groups of unrelated females ($n=4$ to 6 per group) that were formed approximately 14 months prior to the start of this study (Michopoulos, Diaz, & Wilson, 2016). The study was conducted from July through January, spanning the non-breeding and breeding season for this species (Walker, Wilson, & Gordon, 1984). The Emory University Institutional Animal Care and Use Committee approved all procedures in accordance with the Animal Welfare Act and the U.S. Department of Health and Human Services “Guide for Care and Use of Laboratory Animals.”

Macaque social groups are organized by a linear dominance hierarchy; dominant animals display aggression towards subordinate animals, which in turn emit submissive behaviors (Bernstein, 1976; Bernstein & Gordon, 1974; Bernstein, Gordon, & Rose, 1974). With more subordinate status, frequency of harassment increases (Bernstein, 1976) and affiliative interactions with groupmates diminishes (Snyder-Mackler, et al., 2016). Weekly 30-minute observations were conducted throughout the 45-week study period using an established rhesus monkey ethogram that captures the rates and durations of agonistic (aggression and submission), affiliative (proximity and grooming), and anxiety-like behaviors (yawn, body shake) (Jarrell, et al., 2008). Individual dominance ranks within each group were determined by the outcome of dyadic agonistic interactions between individuals (Jarrell, et al., 2008). Because the size of each of the three study groups varied, ranks were converted to relative ranks where, for example, the alpha female in a group of five monkeys was assigned a relative rank of 0.20 (1/5) and the most subordinate female was assigned a relative rank of 1.00 (5/5). As previously described (Michopoulos, Reding, Wilson, & Toufexis, 2012), females ranked 1–2 were classified as dominant ($n=6$) and females ranked 3–6 as subordinate ($n=10$). Dominance ranks were stable during the prior 14 months and during the

45 weeks of the current study, and there were no significant differences in age associated with social status ($p=0.87$), as dominant and subordinate animals were aged 12.10020 ± 1.36 and 12.4 ± 0.75 years, respectively.

2.2 Experimental methods

Animals had access to experimental diets *ad libitum* via previously validated automated feeding stations that allow for quantification of individual caloric intake in socially housed monkeys (Wilson, et al., 2008). Each social group had access to two automated feeders and a computer recorded each feeding event. Validation of the feeding system showed that high-ranking females in these small social groups rarely take a pellet from more subordinate animals and pellets are never discarded (Wilson, et al., 2008). The observation that subordinate females consume more calories in a dietary choice condition underscores that the feeding system is not rank-restricted (Michopoulos, Toufexis, et al., 2012).

The calorie composition of the chow diet (Purina monkey chow, 5038) was 3.45 kcal/g with a distribution of calories of 12% fat, 18% protein, 4.1% sugar-carbohydrate, and 65.9% fiber-carbohydrate. The CDD (D07091204S Research Diets, New Brunswick NJ) had 4.47 kcal/g with a distribution of calories 36% fat, 18% protein, 16.4% sugar-carbohydrate, and 29.6% fiber-carbohydrate. In the obesogenic dietary condition, monkeys were provided access to both the chow and CDD through two separate feeding stations. The rationale for providing access to both the diets is based on well-established data showing that dietary choice sustains intake of high caloric diets (la Fleur, van Rozen, Luijendijk, Groeneweg, & Adan, 2010; Rolls, Van Duijvenvoorde, & Rowe, 1983) and more closely models the human dietary environment.

Animals had been maintained in the dietary choice condition for 14 months prior to the start of this study. At study start, females were maintained in the dietary choice condition for 15 weeks. After this baseline choice phase, the CDD was removed and females only had access to the chow for 15 weeks. Following this chow-only condition, the CDD was reintroduced and females had access to the dietary choice for another 15 weeks ("back-to-choice"). Calorie intake was continually quantified, and body weights and social behavior were measured weekly.

2.3 Statistical Analyses

Data were summarized as mean $\pm$ standard error of the mean (SEM). Because variance of the caloric intake data was not homogenous, data were log transformed prior to analysis. There were no missing data. The main and interaction effects of diet condition (baseline choice vs. chow-only vs. back-to-choice) and status (dominant vs. subordinate) were evaluated with repeated measured analysis of variance (RM-ANOVA) using SPSS Statistics 24 (IBM) to assess the effects of these factors on cumulative calorie intake, body weight, and socioemotional behavior. Similar RM-ANOVAs were run to assess not only the main and interaction effects of diet condition and status, as described above, but also to assess the effects of time (15 weeks) within a dietary condition. Additionally, RM-ANOVA were undertaken to assess the effects of diet condition (baseline choice vs. back-to-choice), status (dominant vs. subordinate), and time (15 weeks) on cumulative calorie intake during these

choice dietary conditions, as well as the intake of CDD and chow separately. The main and interaction effects of diet condition (baseline choice vs. chow-only vs. back-to-choice) and status (dominant vs. subordinate) on the change in body weight during each dietary condition were evaluated with RM-ANOVA. Post-hoc comparisons were made with t-tests using Bonferroni correction. Bivariate correlations were used to determine associations between relative rank, calorie intake, weight change, and socioemotional behaviors across diet conditions. Finally, stepwise multiple regressions were used to assess which factors shown to be associated with body weight change via bivariate correlations during the baseline and back-to-choice conditions best predict weight change. Test results with a $p < 0.05$ were considered significant.

3. RESULTS

3.1 Diet Condition Effects on Calorie Intake

Total cumulative caloric intake varied significantly by phase (Figure 1A; $F_{2,28}=22.52$, $p < 0.001$), with the lowest intake occurring during the chow-only condition compared to both the baseline choice phase ($p=0.039$) and the back-to-choice phase ($p < 0.001$). Greater total calorie intake was observed during the back-to-choice phase compared to the baseline choice phase ($p < 0.001$). This effect of dietary choice increasing caloric intake also varied significantly by social status ($F_{2,28}=4.86$, $p=0.015$). Post-hoc tests revealed that within dominant females, total caloric intake did not vary significantly across the three diet conditions ($p=0.191$; Figure 1A). In contrast, subordinate females significantly reduced total intake when transitioned from the baseline choice to the chow-only phase ($p=0.003$). When transitioned from chow-only to the back-to-choice phase, subordinate females significantly increased total intake ($p < 0.001$). Additionally, subordinate females consumed significantly greater calories during the back-to-choice phase compared to the baseline choice phase ($p=0.001$). In summary, dominant females maintained caloric intake across dietary phases, whereas subordinate females significantly reduced caloric intake when transitioned from baseline to the chow-only phase and subsequently increased caloric intake when transitioned to the back-to-choice phase. This pattern of changing caloric intake across phases by subordinate females was also evident when data were analyzed by weeks (Figure 1B); total calorie consumption showed a significant phase by week by status interaction ($F_{28,392}=2.075$, $p=0.001$). Within subordinate females, total intake varied significantly across dietary phases; however, total intake was not significantly different between subordinate and dominant females during the baseline choice and back-to-choice conditions ($p=0.441$; $p=0.305$, respectively). Moreover, intake was not significantly different between subordinate and dominant females during the chow-only phase ($p=0.070$), despite the significant decline in total intake within the subordinate group when transitioned from the baseline phase to the chow-only phase.

Examination of cumulative calorie intake during the baseline and back-to-choice conditions revealed a significant effect of phase (Figure 2), as more calories were consumed by all females in the back-to-choice condition ($F_{1,14}=39.178$, $p < 0.001$). Consumption of specific diets, independent of social status, also varied significantly during the two choice phases ($F_{1,14}=7.141$, $p=0.018$), with similar amounts of CDD (23319 ± 3123) and chow

(19494±3176) consumed during the baseline choice condition, but more CDD (32860±4182) compared to chow (21920±3035) consumed during the back-to-choice phase ($p=0.039$). There was also a significant status by diet interaction ($F_{1,14}=7.585$, $p=0.016$): subordinate females consumed more calories from the CDD compared to chow (34059±4119 vs. 16507±3780; $p=0.036$), whereas dominant females consumed similar amounts of chow and CDD calories ($p=0.193$). This status-related difference in overall diet preference was associated with status-related differences in consumption of chow and CDD within each phase (Figure 2). During the baseline choice period, subordinates consumed more CDD calories than did dominant females ($p=0.008$), while dominant females ate more chow calories ($p=0.042$). Similarly, in the back-to-choice phase subordinates consumed more CDD calories than did dominant females ($p=0.048$). However, during the back-to-choice phase, chow consumption did not vary by status ($p=0.110$).

Because there was a significant interaction between social status and phase on total caloric intake ($F_{2,28}=4.86$, $p=0.015$), post-hoc tests stratified by social status examined differences in caloric intake of each diet between the baseline and the back-to-choice phases. Within dominant females, the increase in CDD calories from the baseline to the back-to-choice condition did not reach significance ($p=0.051$). Similarly, within dominant females there was no difference in chow intake between the two choice conditions ($p=0.967$). In contrast, subordinate females increased intake of both the CDD ($p=0.002$) and chow ($p=0.012$) from the baseline to the back-to-choice condition, consistent with the observation described above that within subordinate females, the greatest caloric intake (sum of CDD plus chow) occurred during the back-to-choice phase.

Finally, to evaluate whether reintroduction of the CDD impacted diet-specific consumption over the 15 week back-to-choice phase, caloric intake of CDD and chow was stratified by social status and examined by week for the baseline choice and back-to-choice phases (Figure 3). In agreement with the aforementioned difference in diet preference between dominant and subordinate monkeys when cumulative caloric intake was evaluated, the weekly analysis showed a significant interaction between status and diet ($F_{1,14}=6.567$, $p=0.023$), as subordinate females consumed more CDD than chow calories ($p=0.036$), whereas dominant females consumed similar amounts of CDD and chow calories ($p=0.197$). However, there was not a significant interaction when phase ($F_{1,14}<1.00$, $p=0.517$) or phase and weeks ($F_{1,14}=1.006$, $p=0.449$) were added to the model assessing the interaction of status and diet. This weekly analysis revealed that status-related differences in dietary preference were maintained throughout the 15 weeks of each choice phase. Similarly, independent of social status, the intake of CDD and chow did not vary over the 15 weeks of each choice phase ($F_{1,14}=1.464$, $p=0.128$). In summary, dominant females consumed similar amounts of CDD and chow calories, whereas, subordinate females consumed a greater amount of CDD than chow calories. Moreover, these differences in dietary preference between dominant and subordinate females were maintained across weeks within each of the two dietary choice phases.

3.2 Diet Condition Effects on Body Weight

While the change in body weight over the 15 weeks of each dietary condition was affected by phase ($F_{2,28}=3.619$, $p=0.040$), post-hoc comparisons between each of the phases were not significant with Bonferroni correction. Body weight change across the dietary conditions varied significantly by social status ($F_{2,28}=11.413$, $p<0.001$). The body weight change during the baseline choice phase was not different between dominant and subordinate females ($p=0.135$). However, during the chow-only condition, subordinate females lost weight while dominant females gained weight ($p<0.001$; Figure 4A). Finally, during the back-to-choice condition, dominant females showed no change in weight whereas subordinate females gained weight ($p=0.026$; Figure 4A). The significant effect of status during diet cycling was also reflected in absolute body weights across the 15 weeks of each of the dietary conditions (Figure 4B; $F_{28,392}=6.662$, $p<0.001$). Weights progressively increased in dominant females during the chow-only condition and remained stable during the back-to-choice phase. In contrast, weights progressively decreased in subordinates during the chow-only phase and then increased when the CDD was reintroduced. There was no main effect of status on absolute weights ($F_{2,28}=1.169$, $p=0.298$).

Body weight was not significantly different between dominant and subordinate females during the baseline phase, but was significantly different between social groups during the chow-only phase and back-to-choice phase. Therefore, we examined what was predictive of changes in body weight during the chow-only phase and back-to-choice phase. During the chow-only condition, body weight was related to relative rank, with more subordinate females losing more weight ($r_{14}=-0.630$, $p=0.009$). Calorie intake during the chow-only condition did not predict weight loss ($r_{14}=0.444$, $p=0.085$). Interestingly, females that consumed greater calories from CDD during the baseline condition lost more weight when the CDD was removed ($r_{14}=-0.707$, $p=0.002$), whereas females that ate greater calories from chow during the baseline phase lost fewer kilograms ($r_{14}=0.545$, $p=0.029$). Entering these predictors into a stepwise multiple regression model showed that relative rank ($\beta=-0.452$, $p=0.016$) and CDD calories during the baseline choice condition ($\beta=-0.564$, $p=0.004$) predicted more weight loss during the chow-only phase, accounting for 63.5% of variance in weight change. The increase in body weight during the back-to-choice phase was predicted by 1) more subordinate status ($r_{14}=0.554$, $p=0.026$), 2) more CDD calories ($r_{14}=0.708$, $p=0.002$) and fewer chow calories ($r_{14}=-0.726$, $p=0.001$) during the baseline phase, 3) fewer calories consumed during the chow-only phase ($r_{14}=-0.632$, $p=0.009$), and 4) more CDD calories ($r_{14}=0.640$, $p=0.008$) and fewer chow calories ($r_{14}=-0.710$, $p=0.002$) during the back-to-choice phase. The stepwise multiple regression model showed that fewer calories from chow during the baseline choice condition ($\beta=-0.726$; $p=0.001$) predicted significantly more weight gain during the back-to-choice phase, accounting for 63.2% of variance in weight change.

3.3 Diet Condition Effects on Socioemotional Behavior

Cumulative rates and durations of prosocial, agonistic, and anxiety-like behaviors are listed in Table 1. Frequencies and durations of initiating and receiving proximity and grooming did not vary significantly by dietary condition (all $p>0.05$). Rates of initiating proximity to others ($F_{1,15}=4.844$, $p=0.045$) and amount of time receiving grooming from others

($F_{1,14}=5.011$, $p=0.042$) were characteristically lower in subordinate females. Rates of aggression ($F_{2,28}=14.537$, $p<0.001$) and submission directed to others ($F_{2,28}=4.750$, $p=0.017$) varied significantly by phase, with lower rates observed during the chow-only condition. Rates of aggression received were also reduced during the chow-only phase ($F_{2,28}=6.336$, $p=0.005$). Rates of aggression received ($F_{1,14}=22.577$, $p<0.001$) and submission directed to others ($F_{1,14}=21.643$, $p<0.001$) also varied by status, with characteristically higher rates in subordinate females. Rates of anxiety-like behavior did not vary significantly by phase ($F_{1,14}=1.057$, $p=0.361$) but were higher in subordinate females ($F_{1,14}=5.654$, $p=0.032$). There were no status by phase interaction effects on these socioemotional behaviors (all $p>0.05$).

4. DISCUSSION

The current results support our previous finding that a choice dietary environment promotes increased CDD calorie consumption in subordinate female rhesus monkeys (Michopoulos, Toufexis, et al., 2012). In this study, there was no significant difference between dominant and subordinate females in total calories consumed during the either of the dietary choice phases. However, dominant monkeys consumed similar amounts of chow and CDD, whereas subordinates consumed more CDD than chow during the dietary choice conditions. This increased CDD consumption by the subordinate females predicted their weight loss when transitioned to the chow-only phase, and subsequent weight gain during the back-to-choice phase. Together, the data indicate that subordinate, but not dominant, females prefer CDD over chow calories and lose weight in response to removal of the preferred diet. Overall, this study advances our understanding of the relationship between adverse psychosocial experience and ingestive behavior in a dynamic, exogenously manipulated dietary environment.

Our previous studies have shown that subordinates consume more total calories than dominant females in a three-week dietary choice environment with both chow and CDD available (Arce, Michopoulos, Shepard, Ha, & Wilson, 2010; Michopoulos, Toufexis, et al., 2012), corroborating other evidence that stressor exposure promotes increased calorie consumption when CDD is available (see (Razzoli, et al., 2017; Warne, 2009) for reviews). However, in the present study, total caloric intake by subordinates in the two choice conditions was not significantly different from that of dominant females. This difference between previous reports and the current study cannot be attributed to the composition of the CDD, as the CDD used in this study had comparable amounts fat and sugar as the CDD used previously. The small groups of rhesus monkey females used in the previous studies had been together for >7 years, while those used in the present study had been together for only 14 months. It is unclear how this factor could have contributed to the differences in total caloric intake, as dominance ranks in all groups were stable. It should also be noted that while total caloric intake was not different between dominant and subordinate monkeys, dominant females weighed more than the subordinates throughout this study. This result suggests that energy expenditure was different between status groups. However, we were not able to assess total energy expenditure in the current study, thus limiting our ability to interpret how total calorie intake was related to total energy expenditure between status groups.

As found previously (Arce, et al., 2010; Michopoulos, Toufexis, et al., 2012), dominant females consumed similar amount of total calories regardless of diet availability. In contrast, subordinate females were responsive to the changing dietary conditions, consuming more calories during the two dietary choice phases compared to the chow-only condition. This latter observation, though, contrasts with previous findings (Arce, et al., 2010; Michopoulos, Toufexis, et al., 2012) that a history of a dietary choice results in more calorie intake during a chow-only condition. However, the decrease in calorie intake by subordinates during the chow-only condition in the present study is consistent with a large literature in rodents, monkeys, and women that stressor exposure and activation of the hypothalamic-pituitary-adrenal axis produces inappetence when a CDD is unavailable (Heinrichs & Richard, 1999; Jochman, Newman, Kalin, & Bakshi, 2005; Richard, Lin, & Timofeeva, 2002; Tamashiro, et al., 2004). While rodents given alternating availability of chow and CDD consume fewer calories during chow phases and overeat during preferred diet phases (Blasio, et al., 2014; Cottone, Sabino, Steardo, & Zorrilla, 2008, 2009; Eikelboom & Hewitt, 2016; Martire, et al., 2015), stressor exposure was not assessed in those studies. Thus, while diet cycling studies are consistent with the pattern of total calorie intake seen in subordinates in the current study, it does not reflect that of dominant females. Furthermore, total calories consumed by subordinate females during the back-to-choice condition was greater than intake during the initial choice phase, corroborating data from diet-cycled rodents showing that reinstatement of CDD results in more energy intake (Cottone, et al., 2008, 2009; Eikelboom & Hewitt, 2016; Kreisler, Garcia, Spierling, Hui, & Zorrilla, 2017; Martire, et al., 2015).

While dominant animals consumed similar amounts of chow and CDD during both dietary choice phases, subordinate females consumed more CDD than chow calories, supporting previous reports that subordinate females eat more CDD calories than dominant females in a dietary choice condition (Arce, et al., 2010; Michopoulos, Toufexis, et al., 2012). Subordinate, but not dominant, females also consumed more CDD calories during the back-to-choice compared to the baseline choice condition. These data extend findings from diet-cycled rats (Blasio, et al., 2014; Cottone, et al., 2008, 2009; Eikelboom & Hewitt, 2016; Kreisler, et al., 2017; Martire, et al., 2015) showing subordinate females consume more calories from both the CDD and chow following reinstatement of the choice condition. In contrast, and as noted above, calorie intake for dominant females did not change during diet cycling, whether total calories are considered or calories from each of the two diets are evaluated separately. Thus, changes in appetite in response to diet cycling only emerge in animals with a history of chronic psychosocial stressor exposure and are consistent with the notion of stress-induced CDD consumption (Razzoli, et al., 2017; Warne, 2009).

Importantly, social status was associated with dietary preference and changes in body weight in each phase of the study. Both subordination and CDD consumption during the baseline choice condition predicted greater weight loss during the chow-only phase. In contrast, females that preferred chow during the baseline choice phase (i.e. dominant monkeys) did not lose weight upon CDD removal. Body weight gain during the back-to-choice phase was predicted by subordinate status, CDD calories consumed during both choice conditions, and fewer calories consumed from chow. Consumption of obesogenic diets clearly increase body weight (Heber, 2010). Indeed, an effective weight loss strategy is limiting ingestion of saturated fats and processed sugars (Epstein, et al., 2001), nutrients that comprised the CDD

used in the present study. However, it remains unclear how the changing dietary environment impacted energy expenditure in the current study. Energy expenditure may vary by diet condition to influence changes in body weight, because short term, restrictive dieting changes the basal metabolic rate in men and women with obesity (Byrne, Wood, Schutz, & Hills, 2012), and data from diet-cycled rats show activity levels are increased during the chow-only condition relative to the CDD condition (Cottone, et al., 2009).

The chronic stress experience may influence dietary preference by altering neurochemical signaling in the brain and causing reward system deficits so individuals seek out palatable diets (Izzo, Sanna, & Koob, 2005). Reward system dysfunction is observed in individuals with obesity that compulsively overeat (Filbey, Myers, & Dewitt, 2012), and studies show that dopamine D2 receptor (D2R) binding in the striatum is inversely related to body mass index (Wang, Volkow, Thanos, & Fowler, 2004). Decreased baseline D2R binding in the orbitofrontal cortex, an area important for inhibitory control of motivated behavior, is predictive of subsequent increased total calorie intake in female monkeys in an obesogenic dietary environment (Michopoulos, et al., 2016). Reduced D2R binding in cortical-striatal regions may underlie the subordinate monkeys' preferential consumption of CDD over chow during the dietary choice phases, and explain why these animals eat the greatest amount of CDD after reinstatement of dietary choice.

Importantly, a switch to chow from a period of CDD consumption in rodents upregulates stress-related gene expression in the hypothalamus (Martire, et al., 2014). This finding suggests that diet cycling activates the stress axis, whose signals (cortisol and corticotropin-releasing hormone (CRH)) impair dopamine neurotransmission (Izzo, et al., 2005) and alter food salience to increase intake of palatable diets (Warne, 2009). The notion that stress axis function is critical for greater intake of CDD is supported by previous findings that antagonism of CRH receptor 1 reduces total caloric and CDD intake in a dietary choice environment in subordinate females (Moore, Johnson, Higgins, Toufexis, & Wilson, 2015). On the other hand, it is clear that CRH acts on hypothalamic regions to facilitate stress-induced anorexia (Smagin, et al., 1999). This notion is supported by the current finding that only subordinate females show a decrease in caloric intake when cycled to a chow-only environment. Less dietary variety (la Fleur, et al., 2010) and the reduced rewarding value of the chow diet (Andermann & Lowell, 2017) also may contribute to decreased food intake in subordinates in the chow-only condition. Overall, our results support the notion that dietary environment is associated with divergent modulation of appetite by stress signals.

Subordinate females received more aggression and displayed more submissive behavior in each diet condition, as previously described (Michopoulos, Higgins, et al., 2012; Snyder-Mackler, et al., 2016). However, rates of aggression and submission directed to others, as well as rates of aggression received, were significantly lower during the chow-only condition. This finding is in line with behavioral observations of spider monkeys, which revealed that aggression rates and fecal glucocorticoid metabolite levels decreased when availability of the preferred diet was reduced (Rimbach, et al., 2014). Conversely, work with rodents has shown that consumption of a high fat diet induces aggressive behavior in adult male mice and rats (Hilakivi-Clarke, Cho, & Onojafe, 1996), and that long-term consumption of a sugar-sweetened beverage promotes aggressive behaviors in adult male

mice (Choi, et al., 2017). These findings corroborate our current results, which indicate that female monkeys consuming a CDD exhibit increased rates of agonistic behaviors. While diet-cycled rats show increased rates of anxiety-like behavior upon removal of the CDD (Cottone, et al., 2009), rates of anxiety behaviors did not vary across the three diet conditions in the present study. However, the frequency of these anxiety-like behaviors was consistently elevated in subordinate females, indicative of a stress-related phenotype (Arce, et al., 2010; Michopoulos, Higgins, et al., 2012).

In summary, the present results are consistent with previous data showing female monkeys with a history of psychosocial stressor exposure preferentially consume CDD over chow, become mildly inappetent upon removal of the CDD, and subsequently consume even greater amounts of the CDD upon reinstatement of availability. In contrast, dominant females showed no dietary preference and consumed a similar quantity of calories across the changing dietary environments. Within the subordinate females, preference for and increased consumption of CDD was associated with greater weight gain. The data underscore the importance of considering experiential factors in assessing the effects of diet availability on appetite and subsequent changes in body weight. Future studies are needed to assess how exogenous manipulation of the dietary environment may differentially affect dopamine neurochemistry between dominant and subordinate monkeys. In addition, because sex differences in reward pathways have been observed in rodents exposed to a changing dietary environment (Ong, Wanasuria, Lin, Hiscock, & Muhlhausler, 2013), evaluation of neuroadaptations and appetite under different dietary conditions in male monkeys is warranted, particularly given evidence of status-induced differences in D2R availability in the striatum of male monkeys (Morgan, et al., 2002).

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Figure 1.

Mean $\pm$ SEM cumulative total calories consumed (panel A) and average weekly calories (panel B) in each of the three dietary phases for dominant and subordinate females. Symbols denote the main effect of dietary condition, as food intake was significantly different between the three dietary conditions. Letters denote significant differences in intake within subordinate females between phases.

Figure 2.

Mean $\pm$ SEM cumulative calories consumed from chow and the CDD during the baseline choice and back-to-choice phases for dominant and subordinate females. In panel A, double asterisks (**) denote significantly greater total intake during the back-to-choice phase compared to the baseline choice phase. Single asterisks (*) in panel A denote preference for CDD over chow diet within subordinate females. In panels B and C, single asterisks (*) denote a significant difference in calories consumed between dominant and subordinate females. Letters denote significant differences in consumption within subordinate females between dietary phases.

Figure 3.

Mean $\pm$ SEM weekly calories consumed from chow and the CDD during the baseline choice (left panel) and back-to-choice (right panel) phases for dominant and subordinate females.

Figure 4.

Mean $\pm$ SEM body weight change (panel A) and weekly absolute body weights (kg; panel B) during each of the three dietary conditions for dominant and subordinate females.

Asterisks (*) denote significant differences in body weight change between dominant and subordinate females during the chow-only phase and the back-to-choice phase.

Table 1:

emotional behavior for dominant and subordinate females over the 15 weeks of each dietary phase.
 e a “p” reflects a main effect of phase.

Groom Others (Rate)	Groom Receive (Rate)	Proximity Duration	Groom Other Duration	Others Groom Duration*	Aggress Others ^p	Received Aggression ^{*, p}	Submit to Others*	Received Submission ^p	Anxiety*
14 ± 3	13 ± 2	175 ± 26	47 ± 12	44 ± 8	20 ± 9	1 ± 10	3 ± 16	42 ± 14	78 ± 9
8 ± 2	9 ± 2	107 ± 21	26 ± 9	26 ± 7	15 ± 7	25 ± 7	50 ± 12	26 ± 11	88 ± 7
12 ± 3	12 ± 3	148 ± 22	43 ± 8	50 ± 8	21 ± 10	1 ± 8	1 ± 8	35 ± 9	58 ± 12
8 ± 2	8 ± 2	110 ± 17	31 ± 6	25 ± 6	9 ± 7	22 ± 6	36 ± 6	16 ± 7	86 ± 9
11 ± 6	11 ± 2	111 ± 23	27 ± 13	30 ± 6	18 ± 8	2 ± 9	3 ± 16	36 ± 12	69 ± 8
13 ± 4	9 ± 2	111 ± 17	30 ± 10	23 ± 5	18 ± 6	27 ± 7	48 ± 12	32 ± 9	92 ± 6