Effects of long-term diet exposure on decision making in rats

by

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Abstract

Obesity is associated with impaired decision making across a range of choice behaviors including impulsive choice behavior and incentive value. Given that people make approximately 200 food choices each day (Wansink & Sobal, 2007), it is essential to better understand this relationship between obesity and impaired decision making. As such, the current study sought to understand how long-term exposure to diets high in processed fat and sugar affected impulsive choice behavior, devaluation, and food preferences. The results suggested that diet affects impulsive choice behavior. Rats exposed to diets high in processed fat or sugar were more sensitive to changes in delay, a marker of impulsivity. Results from the bisection task indicated that the diet-induced impulsivity could be a result of poor time discrimination. In addition, there were differences in incentive value. All rats successfully devalued rewards, but the high-fat and high-sugar group showed lower overall levels of responding. Further, diet-induced impulsivity could lead to overconsumption of high-fat and high-sugar foods due to differences in food preference. After 9 months on the diets, rats fed a chow and high-sugar diet displayed a sugar preference, while the rats fed a high-fat diet displayed a fat preference. Together, the results suggest that the alterations in impulsive choice and incentive valuation induced by diet could make individuals vulnerable to overeating, and thus obesity, as well as other disorders that are characterized by impulsive choice and deficits in incentive valuation.

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Chapter 1 - Introduction

It is suggested that each person makes approximately 200 food choices each day surrounding when, what, how much, and where to eat (Wansink & Sobal, 2007). Each choice is made by placing a subjective value on each reward, and this value can be affected by a variety of factors including risk, delay, reward type, and amount. Individuals may consider how long it will take to get their food, how much food they will get for the amount they pay, what kind of risk they might be taking (e.g. risk of heart attack or weight gain), and which food they prefer. Low cost, ready to eat foods are tempting to many Americans likely because the food is highly palatable, relatively immediate, and cheap. As such, these high energy, convenient foods constitute a large proportion of the American diet, and overconsumption of these foods can lead to obesity (Bowman & Vinyard, 2004).

The number of food choices made each day poses a challenge for making healthy food choices in all individuals, yet people with obesity may struggle even more. Obesity is associated with several aspects of impaired decision making, creating a potential challenge to make healthy food choices (e.g. Janssen et al., 2017; Rasmussen, Lawyer, & Reilly, 2010; van Meer, Charbonnier, & Smeets, 2016). In fact, a recent review suggests that weight status and age are key factors influencing food decision making, such as food preference and self-control capacity (van Meer et al., 2016). While it is believed that weight status is critical to food decision making, it is recognized that the direction of the relationship is unclear. The correlational nature of these studies demonstrates the need to further investigate the relationship between obesity and impaired decision making. The relationship between obesity and decision making may result from 1) obesity causing impairments in decision making, 2) impaired decision making leading to obesity, or 3) some other factor causing both. Genetics, diet, and physical activity are considered

the key factors in the development of obesity. Given that there has been a rapid increase in the rate of obesity, it is unlikely that genetic changes are driving the obesity epidemic in America (Ogden, Carroll, Fryar, & Flegal, 2015). Rather, it is more likely that environmental/lifestyle factors, such as diet or physical activity, are leading to the rapid increase in obesity (Ng et al., 2014; Popkin, 2001). Diet, in particular, is considered a driver of the obesity epidemic (Swinburn et al., 2011; Swinburn, Sacks, & Ravussin, 2009), and provides a good avenue to better understand the relationship between obesity and impaired decision making.

The direction of the relationship and the influence of diet on decision making is difficult to study in humans because dietary history cannot be controlled, so rodent models can be used to help determine the causal pathways to disease. Diet-induced models of obesity are used to understand how diet affects the brain and behavior through the use of dietary manipulations in rodent models. As such, the current study sought to understand how long-term exposure to a diet high in processed fat or sugar affected decision making using a rodent model with a focus on impulsive choice behavior, devaluation, and food preference. As displayed in Figure 1, it is proposed that exposure to a diet high in fat or sugar (rather than weight status) leads to alterations in impulsive choice, devaluation, and food preference. These alterations in decision making could affect food choice, which would then potentially feed back to dietary intake. Eventually, food choices may drive changes in weight status and/or body composition.

Impulsive choice

Impulsive choice behavior is a trans-disease process (Bickel, Jarmolowicz, Mueller, Koffarnus, & Gatchalian, 2012) thought to underlie several maladaptive behaviors and neurobiological disorders, such as gambling (Alessi & Petry, 2003; Dixon, Jacobs, & Sanders, 2006; Dixon, Marley, & Jacobs, 2003; Petry & Casarella, 1999; Reynolds, 2006), substance

abuse (Bickel & Marsch, 2001; MacKillop et al., 2011; Verdejo-García, Lawrence, & Clark, 2008), obesity (Bickel et al., 2014; Fields, Sabet, & Reynolds, 2013; Jarmolowicz et al., 2014; Rasmussen et al., 2010), and Attention Deficit Hyperactivity Disorder (ADHD; Barkley, Edwards, Laneri, Fletcher, & Metevia, 2001; Bitsakou, Psychogiou, Thompson, & Sonuga-Barke, 2009; Marco et al., 2009; Neef et al., 2005). In impulsive choice tasks, individuals are given a choice between a smaller reward available sooner (smaller-sooner, SS) and a larger reward available later (larger-later, LL). There are two key constructs in impulsive choice tasks: bias and sensitivity. Individuals with an impulsive choice bias show a propensity to choose the SS, which presumably reflects a bias for immediate or shorter delayed rewards. Bias can be measured by assessing the intercept of the choice function. Sensitivity is the degree to which individuals change their behavior when the parameters of the choice task are altered, i.e., the delay or magnitude of reward. Individuals who are sensitive to delay (or magnitude) will show choice functions that have steeper slopes that are characterized as impulsive because the changes in delay (or magnitude) alter the subjective value of reward.

People with obesity and those who eat diets high in fat and sugar are more likely to be impulsive (Bickel et al., 2014; Fields et al., 2013; Jarmolowicz et al., 2014; Lumley, Stevenson, Oaten, Mahmut, & Yeomans, 2016; Rasmussen et al., 2010). Specifically, people with obesity are less willing to wait for the larger reward and thus show greater sensitivity to delay, a marker of impulsive choice (Odum, 2011). This suggests that as delay increases, the subjective value of the reward decreases quickly. While diet-induced models of obesity are widely used to study behavior, there is limited literature investigating the effects of diet on impulsive choice (Narayanaswami, Thompson, Cassis, Bardo, & Dwoskin, 2013; Steele, Pirkle, & Kirkpatrick, under review). One study gave ad libitum access to either a normal diet or a high-fat diet for

eight weeks (Narayanaswami et al., 2013). The results indicated that rats fed a high-fat diet that gained more weight (Obesity Prone) were more self-controlled than rats fed a normal diet and those who were fed a high-fat diet without weight gain (Obesity Resistant). This finding is contrary to what would be expected given that people with obesity are more impulsive (Bickel et al., 2014; Rasmussen et al., 2010).

Steele et al. (under review) sought to address several limitations in the previous study to better understand how diet affects impulsive choice. Both high-fat and high-sugar diets induced an impulsive bias and increased sensitivity to delay. While the high-fat diet resulted in moderate weight gain, weight gain in the high-sugar group was not significantly different from the control group. This suggests that the diets had behavioral and neurological effects before physical signs of obesity, consistent with the proposed model in Figure 1. Following removal from the diets, the high-fat and high-sugar groups showed a reduction in impulsive bias. However, the high-fat and high-sugar groups continued to show greater delay sensitivity compared to controls. This suggests that there were residual effects from the diet.

Both delay and magnitude of the reward affect the subjective value of the reward. Therefore, diet-induced impulsivity could result from delay aversion or deficits in time or magnitude discrimination (see Figure 1). Delay aversion is characterized by an aversion to long delays, and it is a key predictor of ADHD (Bitsakou et al., 2009). The avoidance of long delays has been shown to relate to impulsive choice behavior in that rats who were not tolerant of the long delays made more impulsive choices (Marshall, Smith, & Kirkpatrick, 2014). Therefore, the bias for immediacy induced by diet in Steele et al. (under review) could be a result of delay aversion. In addition to delay aversion, Marshall et al. (2014) investigated how timing abilities (temporal precision and temporal accuracy) were related to impulsive choice. Temporal

precision was measured by the standard deviation of the psychophysical function, which represents the noise in timing. Rats with larger standard deviations have poorer temporal precision. Rats that had poorer temporal precision made more impulsive choices overall (they had a greater impulsive bias), but temporal precision did not predict sensitivity to delay. Additionally, temporal accuracy, measured by the mean of the psychophysical function, did not correlate with impulsive choice. Therefore, temporal precision is critical to impulsive choice. Further, a time-based behavioral intervention improved temporal precision and promoted more self-controlled choice (Smith, Marshall, & Kirkpatrick, 2015). These findings suggest that delay aversion and time discrimination abilities, specifically temporal precision, are a key mechanism of impulsive choice.

The findings surrounding the relationship between reward discrimination and impulsive choice are not as clear. One study found that there was no relationship between impulsive choice behavior and reward discrimination (Marshall et al., 2014), while another study found that rats that had poorer reward discrimination abilities showed an impulsive choice bias (Marshall & Kirkpatrick, 2016). The discrepancy might be a result of task demand and structure, as Marshall and Kirkpatrick (2016) allowed the rats' behavior to determine the reward experienced instead of having experimental manipulations dictate the rewards. Further, a reward-based behavioral intervention improved reward discrimination abilities and promoted more self-controlled choices (Marshall & Kirkpatrick, 2016), which indicates that poor reward discrimination may be a potential mechanism of impulsive choice.

Diet appears to affect both bias and sensitivity to delay, and the effects of delay sensitivity were prolonged, suggesting pronounced effects of diet on sensitivity to delay (Steele et al., under review). To adequately understand how diet affects impulsive choice behavior, it is

essential to know why the individuals have become impulsive, in addition to whether or not the diet leads to impulsivity. Understanding why the deficits in impulsive choice behavior are occurring provides an avenue to improve impulsive choice behavior with a behavioral intervention (Marshall & Kirkpatrick, 2016; Smith et al., 2015). As such, one goal of the current study was to determine how diet affects impulsive behavior, as measured by two impulsive choice tasks – one that manipulates delay and one that manipulates magnitude – and the mechanisms of impulsive choice (i.e., time or reward discrimination). Based on Steele et al. (under review), it was expected that diets high in processed fat or sugar would induce a bias for immediacy and greater sensitivity to delay, as well as deficits in time discrimination abilities; there may also be effects on bias and/or sensitivity to magnitude and reward discrimination abilities.

Devaluation

Just as impulsive choice behavior is associated with maladaptive behaviors, deficits in devaluation underlie maladaptive behaviors such as substance abuse and obesity (Everitt, Dickinson, & Robbins, 2001; Volkow & Wise, 2005). Reinforcer devaluation paradigms require that information about expected outcomes be used to modify behavior in response to a change in value. Specifically, the value of one reinforcer is reduced through satiation, and a choice is given in extinction to determine which reinforcer is wanted more. Adaptive behavior requires that information about the expected outcome be updated to inform decisions. Therefore, individuals should respond more to the lever associated with the reinforcer they did not receive during the satiation period, thus showing sensitivity to the change in reinforcer value.

Three critical constructs involved in devaluation are goal-directed behavior versus habit responding, sensory-specific satiety, and incentive valuation (see Figure 1). The first construct is

the balance between goal-directed behavior and habitual behavior, which determines the degree to which behavior is more flexible or more efficient, is critical (Dickinson, 1985). When the two are out of balance, maladaptive behaviors can occur. For example, following exposure to drugs of abuse, there is evidence of increased habitual control such that the individual is no longer flexible in decision making (Nelson & Killcross, 2006). When behavior is under habitual control, individuals are not sensitive to changes in the value of the outcome and will continue to respond for rewards that have been devalued. The second construct is that the value of specific food should be lower after being sated, a phenomenon known as sensory-specific satiety. Specifically, there is a decrease in pleasantness of a food after satiation (Snoek, Huntjens, van Gemert, de Graaf, & Weenen, 2004). Therefore, responding to the food received during satiation should decrease. The ability to see sensory-specific satiety requires discrimination of the pellet types to adequately learn about the outcomes, and the inability to learn about the outcomes could lead to devaluation deficits. The third construct is incentive valuation. Through experience, individuals assign value to rewards (Dickinson & Balleine, 1994). The more an individual responds for a reinforcer, the higher value attributed to the reinforcer (Epstein, Leddy, Temple, & Faith, 2007). Therefore, habitual responding, sensory-specific satiation, and incentive valuation deficits could result in impairments in devaluation.

It has been proposed that deficits in devaluation resulting from obesity and/or diet are predominantly a result of increased habit responding. Janssen et al. (2017) found that individuals with higher BMIs exhibited less goal-directed behavior, and they propose that individuals with higher obesity scores exhibited automatic behavior. Similarly, men with higher Body Mass Indices (BMI) were poorer at adjusting their behavior after devaluation as evidenced by a smaller change in response rate following satiation (Horstmann et al., 2015). This suggests that obesity

is associated with deficits in devaluation, and it is proposed that this is due to habit responding (Horstmann et al., 2015; Janssen et al., 2017). Research in rats suggests that the deficits in devaluation seen in people with obesity may be a result of diet. It has been found that 28 days of sucrose exposure resulted in an accelerated shift to habitual control (Kendig, Boakes, Rooney, & Corbit, 2013). During the third devaluation test, the rats exposed to sucrose showed similar responding to the devalued and non-devalued lever, while the control group did not show similar responding until the fourth test. In addition, 5 weeks of intermittent access to sweetened condensed milk produced deficits in sensitivity to the devaluation of an outcome as evidenced by similar responding to both rewards following satiation (Furlong, Jayaweera, Balleine, & Corbit, 2014). It is proposed that the diet effects on devaluation are a result of habitual responding (Furlong et al., 2014; Kendig et al., 2013).

The deficits in devaluation could also be a result of sensory-specific satiety. Feeding until sated on a particular food should decrease the pleasantness of that food and rats should shift to eat other food. Epstein, Palugh, and Coleman (1996) found that obese women are not sensitive to sensory-specific satiety, as evidenced by a slower decline in salivation to repeated exposure of a food. In contrast, another study found that women, regardless of obesity, showed sensory-specific satiety (Snoek et al., 2004). However, this study used self-report measures of pleasantness, which could be influenced by demand characteristics and thus explain the discrepancy (Mela, 2001). An investigation of sensory-specific satiety using an animal model indicated that two weeks of exposure to a cafeteria diet resulted in impairments of sensory-specific satiety regardless of whether the rats were on the diet at the time of testing (Reichelt, Morris, & Westbrook, 2014). They propose that the variety in the diet led to impairments in sensory-specific satiety, and that this could lead to overconsumption in general (Reichelt et al.,

2014). Another aspect of sensory-specific satiety is that it requires that individuals discriminate between the two food types. One key goal of the current study was to determine how diet affected discrimination abilities for food types as well as for the delay and magnitude of rewards in the choice task as the diets may induce general deficits in discrimination abilities. Therefore, the investigation of sensory-specific satiety could further elucidate which discrimination abilities are affected by diet.

In addition, deficits in devaluation could be a result of impairments in incentive valuation. Obese children appear to be hyper-responsive to food stimuli both before and after eating, which suggests that there may be deficits in reward valuation in children with obesity (Bruce et al., 2010). In addition, men with higher BMIs showed a smaller change in response rate following satiation, and the authors propose that higher BMIs may be associated with poor adaptation to changes in motivational value (Horstmann et al., 2015). In fact, motivational value predicted food intake better than liking of foods, depicting the strong influence of valuation on food choices (Epstein et al., 2004). Rodent models of devaluation have shown that when rats were given continuous access to sweetened condensed milk, the rats showed devaluation, but they responded less overall, possibly from deficits in valuation processes (Furlong et al., 2014). These findings indicate that incentive valuation is key to devaluation. The current study sought to extend on the current research regarding diet and devaluation to understand how long-term exposure to a diet high in fat or sugar affect devaluation.

Food preference

Another key factor in food choice is food preference (Figure 1). Food preference plays a key role in food choices as individuals are more likely to eat food that they like. Evidence suggests that people with obesity have an increased preference for high-fat and high-sugar foods,

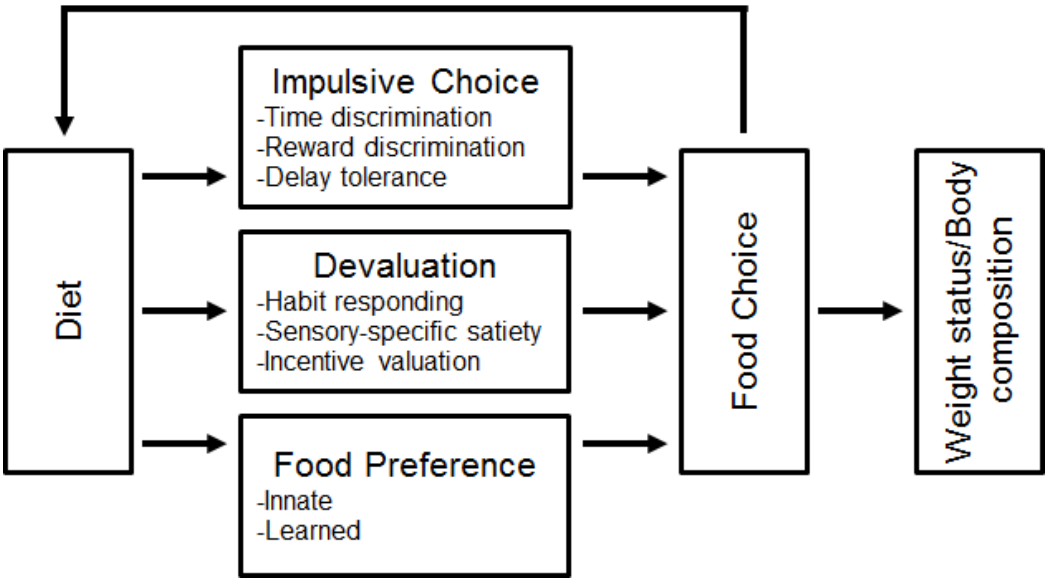
and this could lead to overconsumption of foods high in processed fat and sugar (Mela, 2001). Sugar preference is seen in infants, suggesting that it develops early and may be innate (Birch, 1999). However this predisposed preference for sugar can also be changed with experience (Birch, 1999; Sclafani, 1995). This change in preference is considered a learned preference; learned preferences for a specific type of food can result from repeated exposure to a food (Birch, 1999). These preferences can be strong and persistent (Sclafani, 1995). In fact, preferences seen in children continued into young adulthood (Nicklaus, Boggio, Chabanet, & Issanchou, 2004). While the literature has shown mixed evidence on how food preference is related to weight status, it is thought that fat preference is associated with increased weight (see Cox, Hendrie, & Carty, 2016).

The mixed evidence regarding how food preference is related to weight may be a result of the complexity of food choices. One goal of the current study was to determine how long-term diet exposure can affect preferences for fat and sugar, which is one key aspect of food choice behavior. However, food preferences are only one aspect of food choice being investigated because food choice can be influenced by more than just food preference or liking for a particular substance (Mela, 2001). (Mela) proposes that it is critical to distinguish between liking/preference and incentive value, as both contribute to food choices. Some propose that motivational value is a better predictor of energy intake than liking (Epstein et al., 2004). However, hedonic responses to a particular food can affect incentive valuation (Dickinson & Balleine, 1994). Therefore, the investigation of food preference in conjunction with devaluation could help elucidate how diet affects food choices.

Current study

The current study sought to determine how long-term diet exposure affected choice behavior through an investigation of impulsive choice and the mechanisms of impulsive choice (time and reward discrimination), devaluation, and food preference. Investigating these three behaviors and considering the results together could elucidate the impact of diet on decision making, as these three behaviors are connected and could ultimately affect food choices (see Figure 1). For example, the impulsivity induced by diet (Steele et al., under review) could make individuals more vulnerable to developing maladaptive behaviors associated with impulsive choice and devaluation, such as gambling and substance abuse, later in life. In fact, it is proposed that the ability to devalue rewards is reduced in individuals that are high in impulsivity, suggesting a possible link between devaluation and impulsive choice (Hogarth, Chase, & Baess, 2012). It is thought that persistent or compulsive drug taking could result from the deficits in goal-directed behavior and impulsivity (Belin, Mar, Dalley, Robbins, & Everitt, 2008; Everitt et al., 2008; Verdejo-García et al., 2008). In addition, there is a relationship between reward discrimination abilities and incentive motivation, suggesting another link between the processes involved in impulsive choice and devaluation. Further, food choice behavior is influenced by more than just food preference or liking of a substance, and incentive valuation is considered a key component in food choice behavior (Mela, 2001). Together, these three aspects of choice behavior could elucidate how diet could lead to deficits in decision making when confronted with food choices each day.

Figure 1. Proposed effects of diet on impulsive choice, devaluation, and food preference. Diet exposure is proposed to alter all three processes which in turn affect food choice. Changes in food choices affect dietary exposure, creating a feedback loop which can in turn exacerbate the effects of impulsive choice, devaluation, and/or food preferences in future food choices. The ultimate effects of changes in food choices are to alter weight status and/or body composition.



Chapter 2 - Methods

Animals

Thirty-six male Sprague Dawley rats (Charles River, Portage, MI) arrived at Kansas State University weighing 34-50 g. Only males were used in this study to ensure adequate power. However, future research should investigate potential sex differences. Upon arrival, the rats were housed individually in a dimly-lit (red light) colony room that was set to a reverse 12-hr light:dark schedule (lights off at approximately 7 am). Once body weight measurements were obtained, rats were pseudo-randomly assigned into 3 groups to create roughly similar groups in terms of body weight (Chow: $M = 52.6$, $SE = 1.6$; Fat: $M = 54.4$, $SE = 1.6$; Sugar: $M = 56.0$, $SE = 1.3$).

Dietary manipulation

Initial dietary exposure. The initial dietary exposure consisted of 8 weeks of exposure to the diets without any behavioral testing. All rats received the same number of calories regardless of group through the experiment. To ensure that the rats consumed the food given each day, the number of calories administered was based on the number of calories consumed *ad libitum* throughout development in previous studies (Leibowitz, Lucas, Leibowitz, & Jhanwar, 1991). The number of calories increased each week to match the number of calories in the previous study. However, the composition of calories differed between groups. The control group (Group C) received 100% of the calories from standard chow (4.09 kcal/g). Rats on the high-sugar diet (Group HS) received 60% of the calories from chow and 40% of the calories from a powdered sugar and water mixture (3.94 kcal/g), while rats on the high-fat diet (Group HF) received 60% of the calories from chow and 40% of the calories from hydrogenated vegetable fat (9.3 kcal/g; Jurdak, Lichtenstein, & Kanarek, 2008). The supplements (fat and

sugar) were placed on the floor of the cage. The chow group received 40% of their chow on the floor of the cage to control for the experience of food delivery within the cage.

Three weeks before experimentation, the time allowed to eat the daily ration of supplement and chow was restricted to ensure the rats were motivated to work for food in the experiment and to ensure that the chronic effects of the diet were tested. Rats are usually maintained at 85% of their free feed weight before experimentation. However, one primary goal of the current study was to control for calories. Therefore, the amount of time food was available was restricted, but all rats continued to have the opportunity to eat the same number of calories regardless of group. The rats were allowed 4 hrs to eat the first week of restriction, 3 hrs to eat the second week of restriction, and 2 hrs to eat the final week of restriction and throughout experimentation. The gradual progression was used to reduce the time frame without impacting on total consumption.

Dietary exposure during behavioral testing. The rats received the diets throughout behavioral testing. During behavioral testing, part of the ration of chow was earned in the chambers through 45-mg grain-based pellets (Product #F0165, Bio-Serv, Flemington, NJ). The number of pellets earned in the chambers was subtracted from the ration of chow. After behavioral testing, the remainder of the chow ration was placed on the top of the home cage and the dietary supplement was placed inside the cage.

Food consumption. The bedding was scanned for spillage each day. A formal analysis of spillage was not conducted because the supplements were often mixed with bedding making it difficult to quantify. Generally, Group C and Group HF ate all of their supplement, and Group HS ate a majority of the supplement.

All groups received 60% of their calories in chow placed in the food hopper on top of the cage each day, and chow leftover in the food hopper was measured to determine food intake. Food intake during behavioral testing was not analyzed because part of the daily food ration was received in the apparatus making it difficult to quantify consumption. One week prior to behavioral testing, the groups differed in their chow intake, $F(2, 270) = 22.44$, $p < .001$. Group HS ($M = 11.14$, $SE = 0.33$) ate more chow than Group HF ($M = 9.31$, $SE = 0.34$), and Group HF ate more chow than Group C ($M = 7.07$, $SE = 0.42$).

Body composition

The rats were weighed at least five times per week throughout experimentation. As an additional measurement of body composition, body fat percentages were obtained using a Lunar PIXImus small animal densitometer (Lunar-General Electric, Madison, WI). A measurement of body fat (and lean muscle) composition was obtained after 6 weeks on the diet and following experimentation after 9 months on the diet. The densitometer is specific for small animals (i.e. mice), so only smaller targeted regions could be examined. As such, the measurements focused on abdominal fat stores because visceral adipose tissue in the abdomen increases the risk of obesity-related diseases (Bjorndal, Burri, Staalesen, Skorve, & Berge, 2011). The region of interest spanned the abdomen from the second to last rib to the top of the pelvis. Isoflurane as an anesthetic was used to ensure an accurate measurement was obtained without movement from the animal. Isoflurane was administered in an induction chamber at a concentration of 3-5% and a flow rate of 500 ml/min. The rats were then transferred to a face mask with a concentration of 1-3% and a flow rate of 500 ml/min. An adequate level of anesthesia was confirmed by checking the pedal withdrawal reflex and mild tail pinch responses. Once the rat was anesthetized, they were placed on the platform of the densitometer and began imaging, which

took approximately 4-5 mins. As soon as the image was obtained, the rat was placed in a recovery cage. Anesthesia was administered for 5-10 min for each imaging session.

Apparatus

The behavioral tasks were conducted in 24 operant chambers (Med-Associates, St. Albans, VT), each housed within a sound-attenuating, ventilated box (74 x 38 x 60 cm). Each operant chamber (25 x 30 x 30) was equipped with a stainless steel grid floor; two stainless steel walls (front and back); and a transparent polycarbonate side wall, ceiling, and door. Two pellet dispensers (ENV-203), mounted on the outside of the front wall of the operant chamber, delivered 45-mg food pellets (Product #F0165, Bio-Serv, Flemington, NJ) to a food cup (ENV-200R7) that was centered on the lower section of the front wall. Head entries into the food magazine were transduced by an infrared photobeam (ENV-254). Two retractable levers (ENV-112CM) were located on opposite sides of the food cup. The chamber was also equipped with a house light (ENV-215) that was centered at the top of the chamber's front wall, as well as two nose-poke key lights (ENV-119M-1) that were each located above the left and right levers. Water was always available from a sipper tube that protruded through the back wall of the chamber. Experimental events were controlled and recorded with 2-ms resolution by the software program MED-PC IV (Tatham & Zurn, 1989). For the devaluation task, the left and right pellet dispensers delivered either a 45-mg high-fat pellet (Product #F07373, BioServ, Flemington, NJ) or a 45-mg sucrose pellet (Product #F06233, BioServ, Flemington, NJ).

Procedure

Rats received a series of tasks to determine how chronic exposure to a diet high in processed fat or sugar affected impulsive choice, devaluation, and food preference (Figure 2). Behavioral testing began with an impulsive choice task followed by the discrimination task

associated with that impulsive choice task (e.g. delay manipulation of the impulsive choice task followed by the bisection task or magnitude manipulation of the impulsive choice task followed by the reward sensitivity task). Between the impulsive choice task and the discrimination task, a buffer task was completed to reduce side biases and carry-over effects. After the first set of impulsive choice and discrimination tasks, the rats completed another buffer task and the lever assignment was switched before beginning the next set of impulsive choice and discrimination tasks. The order of the impulsive choice tasks was counterbalanced such that half of the rats received the delay manipulation of the impulsive choice task first and the other half of the rats received the magnitude manipulation of the impulsive choice task first. Following the impulsive choice and discrimination tasks, all rats completed the devaluation task. To conclude, a preference test was conducted to determine how diet affects food preference. The tasks were administered in this order, instead of counterbalancing everything, because there was not enough power to test order effects. In addition, the impulsive choice and discrimination tasks were administered first to avoid exposure to different diets.

Impulsive choice. The impulsive choice task was used to determine the rats' willingness to wait for the larger reward. Two impulsive choice tasks were used. One task manipulated the delay to the SS reward, while the other task manipulated the magnitude of the LL reward. All rats completed pre-training, then they completed both tasks. The order of the impulsive choice task was counterbalanced across rats so that half completed the delay manipulation first and half completed the magnitude manipulation first.

Pre-training. During the first training session, rats received magazine training and lever-press training. The magazine training consisted of delivery of 60 food pellets into a food cup through a random time 60-s schedule. Following magazine training, lever-press training

rewarded lever presses with a fixed-ratio (FR) 1 schedule of reinforcement. Left and right levers were trained separately in 6 sub-blocks of 10 food deliveries resulting in a total of 30 pellets per lever. Following the first training session, the rats continued lever-press training during three sessions. First, lever pressing was rewarded on a FR1 schedule of reinforcement. Left and right levers were trained separately in four sub-blocks (two blocks per lever). Following the FR1 training, both levers were inserted and lever pressing was rewarded on a random ratio (RR) 3 schedule of reinforcement, followed by an RR5 schedule of reinforcement. For both the RR3 and RR5 block, each of the four sub-blocks consisted of 5 food deliveries per a lever.

Training. The impulsive choice tasks were modifications of the tasks used in Garcia and Kirkpatrick (2013) to parse out sensitivity to magnitude and delay. Each session consisted of a randomly intermixed series of free choice and forced choice trials. At the beginning of each session, there was a 10-s interval preceding the first trial. On free choice trials, both the left and right levers were inserted into the chamber, corresponding to smaller-sooner (SS) and larger-later (LL) outcomes, with lever assignments counterbalanced across rats. Upon selection of one of the outcomes via a lever press, the other lever was retracted. The choice initiated a delay until food was available to be delivered; the first lever press following this delay caused the lever to retract, food to be delivered, and a 60-s intertrial interval (ITI) to begin. Forced choice trials were identical to free choice trials, except that only one lever was inserted into the chamber. Each session consisted of 54 free choice trials, 14 SS forced choice trials, and 14 LL forced choice trials, and lasted until all 82 trials have been completed or approximately 2 hr had elapsed. All rats completed two impulsive choice tasks, one that manipulated SS delay and one that manipulated LL magnitude. The procedures were counterbalanced across groups such that half of the rats in each group received the delay manipulation first and the other half received the

magnitude manipulation first. Prior to switching to the second impulsive choice task, the SS/LL lever assignments were switched and the rats completed the buffer task described below to reduce carry-over effects and side biases.

For the delay manipulation, the delay to the SS reward was manipulated. The SS choice always delivered 1 pellet and the LL reward always delivered 2 pellets. There were 45 sessions. The LL delay was 30 s and the SS delay increased every 15 sessions: 5, 10, and 20 s.

For the magnitude manipulation, the magnitude of the LL reward was manipulated. The SS delay was always 10 s and the LL delay was always 30 s. There were 45 sessions. The SS reward was 1 pellet and the LL reward increased every 15 sessions: 1, 2, and 4 pellet(s).

Temporal Bisection. A temporal bisection task, modified from Church and Deluty (1977), was used to test the rats' ability to discriminate different signal durations because poorer ability to discriminate delays predicts more impulsive behavior (Marshall et al., 2014). After completing the delay manipulation of the impulsive choice task, a buffer task was administered and then rats began the bisection task. Rats completed training sessions where the levers were associated with a long or a short duration. After learning the association, rats received 10 testing sessions where intermediate delays were presented, and the rats classified the delay as short or long.

Training. Rats received initial training with a 4-s short and a 12-s long houselight signal. Each trial began with the onset of the houselight that lasted for either the short or long duration. Following the signal, both levers were inserted and a choice response was collected. Correct responses were followed by a 1-pellet food delivery and then a 15-s ITI. Incorrect responses were followed by a correction trial that were composed of a 5-s ITI and a repeat of the previous trial until a correct response was made and food was delivered. Sessions lasted for a maximum

of 2 hr. Each session delivered 160 trials in four blocks of 40 trials each. Each block consisted of 20 long and 20 short trials. Training continued until the rats achieved a group criterion of at least 80% correct on two consecutive sessions, which took 11 sessions for those who received this task first and 13 sessions for those who received this task second. The correct response for the short 4-s duration was the same lever as the SS lever and the correct response for the 12-s duration was the same lever as the LL lever in the delay impulsive choice task.

Testing. Once training was completed, the rats received a series of test sessions with non-reinforced durations following a geometric progression intermixed with normal training trials: 4, 5.26, 6.04, 6.93, 7.94, 9.12, and 12 s signals. Therefore, the middle duration was the geometric mean of the shortest and longest signal duration, which has been found to be the point of bisection (Church & Deluty, 1977). Test trials were administered in the same fashion as normal training trials, except that responses were not followed by reinforcement and there were no correction trials. The subjective perception of the length of the signal duration was tested, so there were no correct responses to test trials. Each of the four blocks consisted of 1 test of each duration intermixed among the 40 training trials so that each duration was administered 4 times in a session. There were 10 test sessions. The tests produced a psychophysical function relating the signal duration to the proportion of long responses.

Reward sensitivity. The reward sensitivity test involved the simultaneous presentation of both levers, for which lever pressing was reinforced on variable-interval (VI) schedules of reinforcement. Following the magnitude manipulation of the impulsive choice task, rats completed the buffer task and then began the reward sensitivity task. The reward sensitivity task consisted of a concurrent VI-VI task with two VI 30 s schedules of reinforcement, in which food became available to be delivered *t* s following lever insertion. The values of *t* were drawn from

independent negative exponential distributions with means and variances of 30 s to promote constant rates of responding. Food was delivered following the first lever press after *t* s had elapsed on that lever. The schedule of food deliveries on the two levers were independent.

The primary manipulation within the concurrent VI-VI task was the reward magnitude on the VI 30-s schedule; with the "large" lever on the same side as the LL outcome in the magnitude impulsive choice task. On the “small” lever, one pellet of food was delivered following completion of the VI 30. Alternatively, on the “large” lever, the reward magnitude increased across phases: 1, 2, and 4 pellet(s). Each session lasted until approximately 200 food pellets were delivered or until 2 hr had elapsed. Rats were trained until the rats exhibited stable behavior. Phase 1 lasted for 11 sessions for rats who received this test first and 13 sessions for rats who received this test second. Subsequently, Phases 2-3 lasted for 5 sessions.

Buffer task. A modification of the lever press training was used in between each task to minimize side biases and the carryover effects from one task to another. Wang, Marshall, and Kirkpatrick (under review) found that the buffer task resulted in minimal cross-task interference and eliminated side biases. It consisted of three sessions. The first session delivered FR1 → RR3 → RR5 schedules where each schedule was trained for one block with 20 reinforcers earned on each lever, constituting three blocks in total. The second and third session consisted of three blocks of RR5 with 20 reinforcers on each lever per block. A 5-min inter-block interval (IBI) was delivered for both sessions.

Devaluation. The devaluation task was used to determine how diet affected the ability to devalue rewards. It is often used as a measure of incentive learning after a motivation has changed (Balleine, 1992). The devaluation task consisted of two pre-training session followed by 4 training sessions. After training the lever-pellet association, a testing session was

administered. Following the first testing session, two session of training were administered before beginning the second testing session.

Pre-training. Following the impulsive choice and discrimination tasks, two sessions of lever press training were used for rats to learn the lever and pellet associations. Only one type of pellet was delivered each session (AB; A = sugar, B = fat). Each lever was associated with one type of pellet throughout training. Lever-press training rewarded lever presses with a fixed-ratio (FR) 1 schedule of reinforcement.

Training. The rats were given one session of training for four days in 2 blocks of 2 sessions (ABBA). In the first block, one lever was paired with a pellet type to establish the reinforcer/lever association. In the second block, the other lever was paired with the other pellet type. This training mirrored the reward sensitivity task in that a VI 30-s schedule of reinforcement was used, in which food became available to be delivered *t* s following lever insertion. The values of *t* were drawn from independent negative exponential distributions with means and variances of 30 s. One food pellet was delivered following the first lever press after *t* s has elapsed on that lever. Each session lasted until approximately 80 trials had been delivered or until 2 hr had elapsed.

Testing. The rats completed two choice tests, each of which were preceded by a 1-hr satiation period. During the satiation period, the rats received access to a total of 640 pellets of one of the pellet types for 60 min in the experimental chamber. After 3 minutes, 4 pellets were delivered every 15 s. For the first test, half of the rats received access to sucrose pellets and the other half received access to high-fat pellets during the satiation period. A 30 min break following the satiation period commenced where the rats were moved to their home cage, and food intake was measured. Then, the rats were given a choice test in extinction with no pellets

earned for either response. The test was a free-operant procedure where both levers were inserted and rats were allowed to repeatedly respond until the 20 min test session was completed. After the first choice test, the rats were given two retraining sessions, one for each lever-pellet combination (BA). Following retraining, the rats were given a second choice test. This test was identical to the first except that the rats that had high-fat pellets devalued now had sucrose pellets devalued, and those that had sucrose pellets devalued now had high-fat pellets devalued.

Preference. A restricted access consumption test was used to determine how dietary history affected food preference. Following the devaluation task, each rat completed the preference test which consisted of three days of testing: an exposure period and two consumptions tests. For the exposure period, the rats were placed in a breeder cage (18.25" x 12" x 6.25") with two bowls, randomly assigned to a corner of the cage. There was 1 g of each supplement (fat and sugar) placed in a bowl. The rats were given an opportunity to explore the cage and consume both supplements. The rats were removed after they consumed all of the supplements or after 10 min elapsed. On the second and third day of testing, each rat went through a consumption test, where rats were given the choice between the two supplements (fat and sugar). The location of the bowls was switched each day to address for any potential side biases. They were given 1 min to eat from the two bowls, which contained 3 g of each supplement. Once 1 min had elapsed, the rat were removed from the cage, and any remaining supplement was weighed.

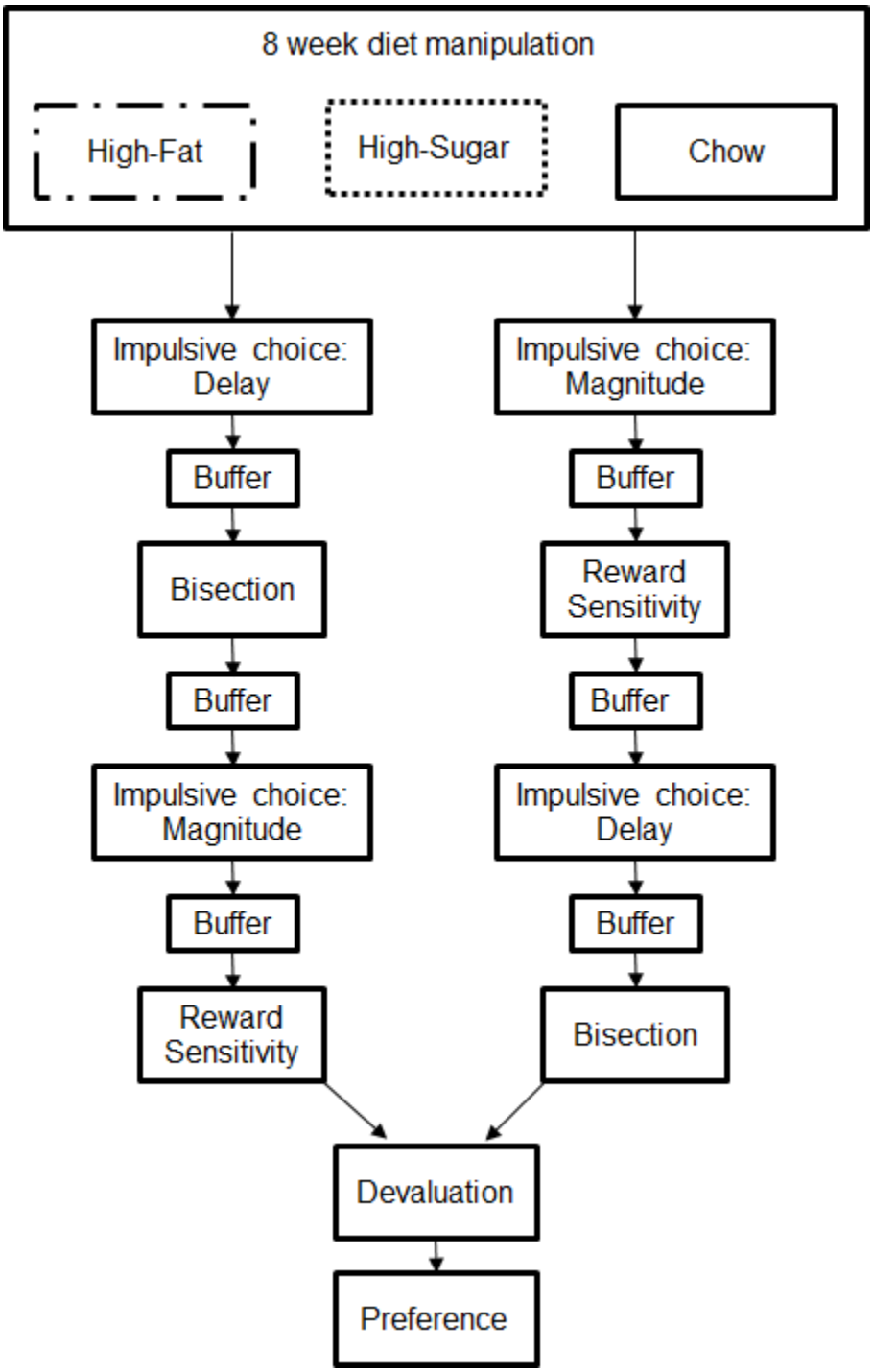
Data analysis

The raw data were imported into MATLAB 2016a (MathWorks). Repeated measures regressions were conducted for each task (see Results for details). A theory-driven approach was used such that the hypothesized effects were tested as fixed effects, and the Akaike Information

Criterion (AIC) was used to determine the best random effects structure. All categorical variables were effect-coded so that the coefficients summed to 0. Subsequently, post-hoc comparisons were conducted to compare the high-fat and high-sugar group to the chow group using the coefficient test function in MATLAB. As a measure of effect size, the unstandardized regression weights (*b*) and the associated 95% confidence intervals are reported. The estimates from the logistic regressions were converted into proportions to help with interpretability, and the proportions appear in the figures. The error bars in the figures are the standard error (SE) of the estimates from the model, and they were determined using the predict function in MATLAB.

It was proposed to investigate individual differences to determine if diet changed the expression of individual difference correlation patterns. Individual differences in impulsive choice are related to individual differences on the discrimination tasks, such that individuals who are more impulsive are poorer at discriminating delay and magnitude (Marshall & Kirkpatrick, 2016; Marshall et al., 2014). However, correlations between the impulsive choice tasks and the discrimination tasks were not conducted due to poor reliability within the impulsive choice tasks as measured by a Cronbach's alpha test (magnitude: $\alpha = .32$; delay: $\alpha = .74$). While the overall alpha level for the delay manipulation of the impulsive choice task was acceptable, the reliability within the phases was poor (5-s: $\alpha = .58$; 10-s: $\alpha = .41$).

Figure 2. Order of procedures experienced by sub-groups of rats within each dietary condition. Rats received the impulsive choice and discrimination tasks in a counterbalanced order and then all rats experienced devaluation and food preference testing at the end of the experiment.



Chapter 3 - Results

Body composition

Body weight. A repeated measures linear regression was used to predict body weight (g). The best fitting model included age (mean centered to address for multicollinearity and log transformed to address violations of normality) as a fixed effect, and intercept and age as random effects. There was a significant main effect of age, such that rats gained weight as they aged, $t(7464) = 39.36$, $p < .001$, $b = 154.37$ [146.68, 162.06] (Figure 3). The best fitting model did not include group suggesting that their dietary condition was not a good predictor of their body weight.

Percent body fat. A repeated measures linear regression was used to predict the percent body fat in the abdomen (log transformed to normalize the data) obtained through the Lunar PIXImus. The best fitting model included the Group × Time interaction and both main effects as fixed effects. Intercept was included as a random effect. Group was a categorical predictor (effect coded) and time was a continuous predictor (mean centered to reduce multicollinearity). Measures were obtained after about 1.5 months and 9 months on the diet.

There was a significant main effect of group, such that Group HF, $b = 21.59$, had a higher percent of body fat than Group C, $b = 12.15$, $t(66) = 8.91$, $p < .001$. Group HS also had higher percent body fat, $b = 15.89$, compared to Group C, $b = 12.15$, $t(66) = 4.16$, $p < .001$. There was also a significant Group × Time interaction (see Figure 4). However, coefficient comparisons indicated that the change in percent body fat in Group HF, $b = .60$, did not differ from Group C, $b = 0.57$, $t(66) = 1.73$, $p = .09$, nor did Group HS, $b = 0.54$, differ from Group C, $b = 0.57$, $t(66) = 1.51$, $p = .14$. Overall, the high-fat and the high-sugar rats had more body fat than the chow rats, but the changes in body fat over time did not differ between the groups.

Impulsive choice

A repeated measures logistic regression was used to predict the proportion of LL choices made during the impulsive choice tasks. The primary dependent measure of impulsive choice tasks was the individual choices for the SS and LL outcomes (SS = 0, LL = 1). Possible fixed effects included group (effect coded), the parameter being manipulated (SS delay or LL magnitude), and the interaction between the two. The approach used by Wileyto, Audrain-McGover, Epstein, and Lerman (2004) was adapted to help parse out bias versus sensitivity to better isolate the mechanisms of dietary effects on choice behavior. As such, the slope for each task represented the sensitivity to the manipulated parameter (magnitude or delay), and the intercept represented the bias in choice behavior. The SS delay was scaled so that the intercept represented a 0-s delay for the SS reward (SS/LL). Therefore, the intercept represents a bias for the immediacy. The LL magnitude was scaled so that the intercept represented a bias for the large reward (SS/LL – SS/maximum LL). The model for both tasks included Group × LL magnitude/SS delay as a fixed effect and intercept as a random effect.

Delay manipulation. Overall, rats showed a bias for the SS reward, $b = 0.06$, $t(72572) = -13.53$, $p < .001$. There was a main effect of group, and post-hoc comparisons indicated that Group HS, $b = 0.04$, showed a larger bias for the immediate reward compared to Group C, $b = 0.09$, $t(72572) = 2.17$, $p = .03$. However, Group HF, $b = .05$, did not differ from Group C, $t(72572) = 1.37$, $p = .17$, although they did have a trend towards a greater SS bias. All groups showed a positive slope with changes in the SS delay, such that as the SS delay increased, the rats made more LL choices, $b = 6.33$, $t(72572) = 115.73$, $p < .001$. The groups differed in their sensitivity to the changes in the delay to the smaller reward as evidenced by a significant Group × Delay interaction (see Figure 5A). Specifically, Group HF, $b = 6.26$, had a steeper slope than

Group C, b = 5.76, indicating greater delay sensitivity, $t(72572) = 3.70$, $p < .001$. Similarly, Group HS, b = 6.96, had a steeper slope than Group C, $t(72572) = 8.91$, $p < .001$. Overall, Group HS had a greater immediacy bias and sensitivity to delay, while Group HF displayed a greater sensitivity to delay.

Magnitude manipulation. Overall, rats showed a bias for the LL reward, b = 0.64, $t(70423) = 4.48$, $p < .001$. There was no main effect of group, and coefficient tests indicated that Group HS, b = 0.69, did not differ in their bias for the large reward, compared to Group C, b = 0.66, $t(70423) = 0.44$, $p = .66$. Group HF, b = 0.57, also did not significant differ in their bias for the large reward compared to Group C, b = 0.66, $t(70423) = 1.16$, $p = .25$. All groups showed a positive slope with changes in the LL magnitude, such that as the LL magnitude increased, the rats made more LL choices, b = 6.33, $t(70423) = 111.32$, $p < .001$. The groups differed in their sensitivity to the changes in the magnitude of the large reward as evidenced by a significant Group × Magnitude interaction (see Figure 5B). Specifically, Group HF, b = 4.52, had a shallower slope than Group C, b = 5.54, indicating lower sensitivity to changes in magnitude, $t(70423) = 8.87$, $p < .001$. However, Group HS, b = 5.55, did not differ in their sensitivity to changes in magnitude, compared to Group C, b = 5.54, $t(70423) = .10$, $p = .92$. Overall, Group HF was less sensitive to changes in magnitude.

Discrimination

Temporal Bisection. A repeated measures logistic regression was used to predict the proportion of long responses during the bisection task (short = 0, long = 1). The best fitting model included Group × Signal Duration and both main effects as fixed effects. Random effects included intercept and signal duration. Group was a categorical predictor (effect coded). Signal duration was mean centered at the geometric mean because it is the typical point of bisection

(Church & Deluty, 1977). Signal duration was scaled in proportion to the long signal duration (Duration/Maximum Duration).

There was a significant main effect of signal duration, such that as the signal duration increased the rats increasingly responded that the signal was long, $t(7632) = 13.62$, $p < .001$, $b = 3.96$ [3.39, 4.53]. There was also a significant Group × Signal Duration interaction (see Figure 6). Coefficient tests indicated that the proportion of long responses made by Group HF across signal durations significantly differed from Group C, $t(7632) = 2.48$, $p = .01$. Specifically, Group HF showed a shallower slope, $b = 0.26$, compared to Group C, $b = 0.41$. The change in proportion of long responses for Group HS, $b = 0.32$, did not significantly differ from Group C, $b = 0.41$, $t(7632) = 1.52$, $p = .13$. Overall, the groups did not differ in temporal accuracy, but Group HF showed poorer temporal precision as evidenced by the shallower slope.

Reward sensitivity. A repeated measure logistic regression was used to predict the proportion of large responses during the reward sensitivity task (small = 0, large = 1). The best fitting model included Group × Magnitude and all lower effects as fixed effects. Random effects included intercept and magnitude. Group was a categorical predictor (effect coded) and magnitude was a continuous predictor. Magnitude was scaled so that the intercept predicted choice when the small and large magnitudes were equal (S = L).

There was a significant main effect of group. Post-hoc comparisons indicated that the proportion of large responses made by Group HS, $b = 0.58$, was significantly more than Group C, $b = 0.49$, $t(727806) = 2.33$, $p = .02$. This bias for the lever associated with the large reward even when the pellet amounts were identical suggests Group HS had a side bias. The bias for the larger reward for Group HF, $b = 0.53$, did not significantly differ from Group C, $b = 0.49$, $t(727806) = 0.93$, $p = .35$. There was a significant main effect of magnitude, such that as the

magnitude of the large lever increased, the rats pressed the large lever more often, $t(727806) = 5.64$, $p < .001$, $b = .57$ [.37, .76]. The sensitivity to changes in the magnitude did not differ between groups. The Group × Magnitude interaction is depicted in Figure 7. Coefficient comparisons indicated that the proportion of large responses made by Group HS, $b = 0.34$, as a function of magnitude did not differ from Group C, $b = 0.78$, $t(727806) = 1.81$, $p = .07$. Similarly, the change in proportion of large responses for Group HF, $b = 0.58$, did not significantly differ from Group C, $b = 0.78$, $t(727806) = 0.84$, $p = .40$.

Devaluation

A repeated measures Poisson regression was used to predict the number of responses during the first five minutes of the extinction choice test. The best fitting model included Group × Lever and the main effects of group and lever as fixed effects. Random effects included intercept. Group and lever were categorical predictors (effect coded). There was a significant main effect of lever, such that the rats made more responses to the non-devalued lever, $b = 101.32$, than the devalued lever, $b = 42.36$, $t(66) = -29.31$, $p < .001$, showing that all groups successfully devalued the reward. There was also a significant Group × Lever interaction (see Figure 8B). Planned comparisons indicated that the number of responses made to the devalued lever by Group HF, $b = 30.10$, was significantly fewer than Group C, $b = 47.60$, $t(66) = 2.28$, $p = .03$. The number of responses to the devalued lever for Group HS, $b = 53.04$, did not significantly differ from Group C, $b = 47.60$, $t(66) = 0.55$, $p = .59$. The number of responses made to the non-devalued lever by Group HF, $b = 67.49$, was significantly fewer than Group C, $b = 167.40$, $t(66) = 4.66$, $p < .001$. The number of responses to the non-devalued lever for Group HS, $b = 92.07$, was significantly fewer than Group C, $b = 167.40$, $t(66) = 3.08$, $p < .001$. However, these differences in responses may be attributed to Group C responding more during

training. The average number of responses over 5 mins during training was significantly higher for Group C, $b = 23.18$, compared to Group HS, $b = 12.49$, $t(138) = 3.13$, $p = .002$, and Group HF, $b = 7.36$, $t(138) = 5.81$, $p < .001$ (Figure 8A). In addition, there was a main effect of pellet, $b = 6.80$, $t(138) = -122.16$, $p < .001$, suggesting that the rats responded differently for fat and sugar (Figure 8A) in that all groups responded less for the fat pellet, ps $< .001$. Overall, rats devalued the outcome regardless of dietary exposure.

Preference

During the exposure period (test number 1), there were no significant differences in consumption between Group HF, $b = .52$, and Group C, $b = .44$, $t(33) = 1.52$, $p = .14$, nor Group HS, $b = .42$, and Group C, $t(33) = 0.33$, $p = .75$. A repeated measures linear regression was used to predict the preference during the consumption tests of the preference task. The dependent variable was the log odds of fat consumed to address violations of normality. The log odds of fat consumed was computed by taking the natural logarithm of the grams of fat consumed to the grams of sugar consumed, and a value of .5 was added to each to account of exclusive consumption. The best fitting model included Group × Test Number and both main effects as fixed effects. Intercept was included as a random effect. Group was a categorical predictor (effect coded) and test number was a continuous predictor. Test number was scaled so that the intercept represented preference during the second test.

There was a significant main effect of group, such that Group HF, $b = 0.70$, consumed more fat than Group C, $b = 0.30$, $t(66) = 4.09$, $p < .001$. Group HF showed a preference for fat as indicated by an estimate above .5, while Group C showed a preference for sugar. Group HS also showed a preference for sugar, $b = 0.17$, and this preference did not significantly differ from Group C, $t(66) = 1.78$, $p = .08$. While the best fitting model included Group × Test Number, the

interaction was not significant (see Figure 9). Post-hoc comparisons indicated that the consumption by Group HF, $b = 0.08$, across time did not differ from Group C, $b = -0.62$, $t(66) = 1.32$, $p = .19$. The change in consumption over time for Group HS, $b = -0.95$, did not significantly differ from Group C, $b = -0.62$, $t(66) = 0.61$, $p = .54$. Overall, Group HS and C showed a preference for sugar, while Group HF showed a preference for fat.

Figure 3. Mean body weight (g) for each group as a function of age. PND = postnatal day. HF = high-fat; HS = high-sugar; C = chow.

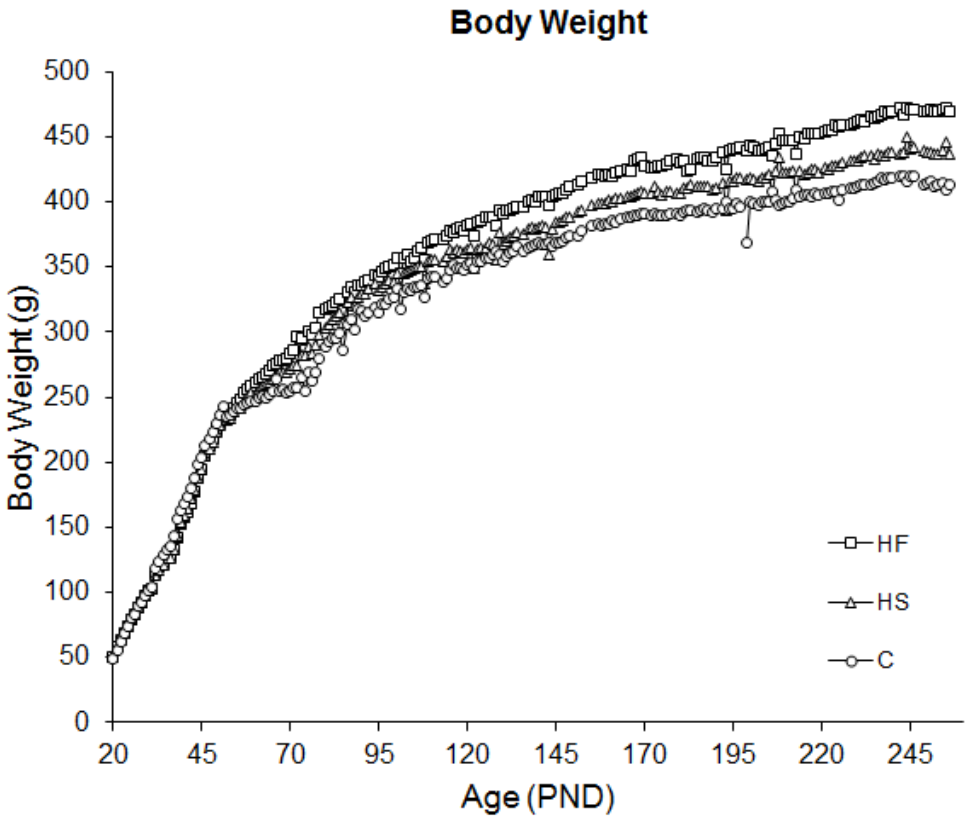


Figure 4. Mean (± SE of the estimates) percent body fat in the abdomen for each group as a function of time on the diet. HF = high-fat; HS = high-sugar; C = chow.

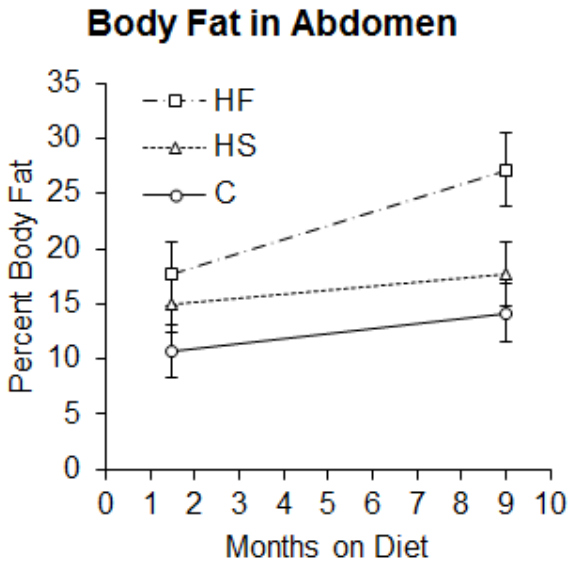


Figure 5. Mean (± SE of the estimates) proportion of LL choices for each group as a function of phase parameter on the A) delay manipulation of the impulsive choice task and B) magnitude manipulation of the impulsive choice task. HF = high-fat; HS = high-sugar; C = chow.

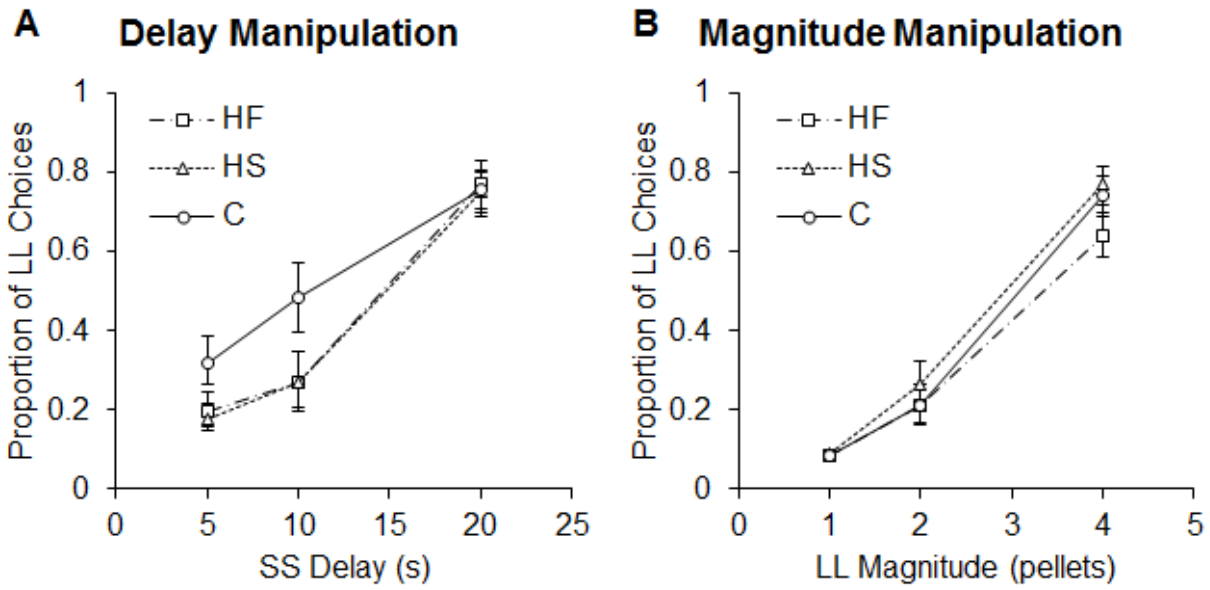


Figure 6. Mean (± SE of the estimates) proportion of long responses on the temporal bisection task for each group as a function of signal duration. HF = high-fat; HS = high-sugar; C = chow.

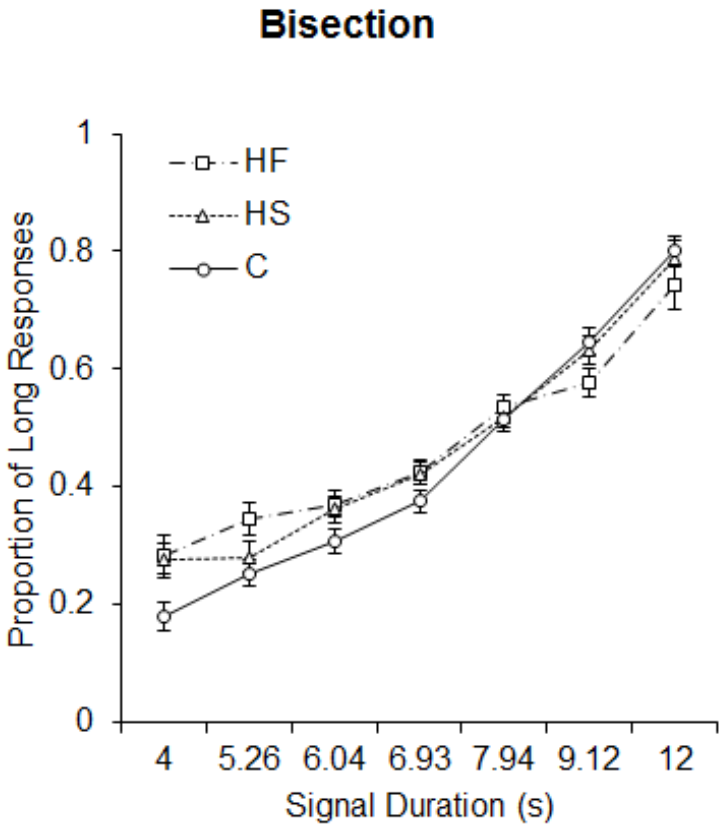


Figure 7. Mean (± SE of the estimates) proportion of large responses for each group as a function of the large magnitude. HF = high-fat; HS = high-sugar; C = chow.

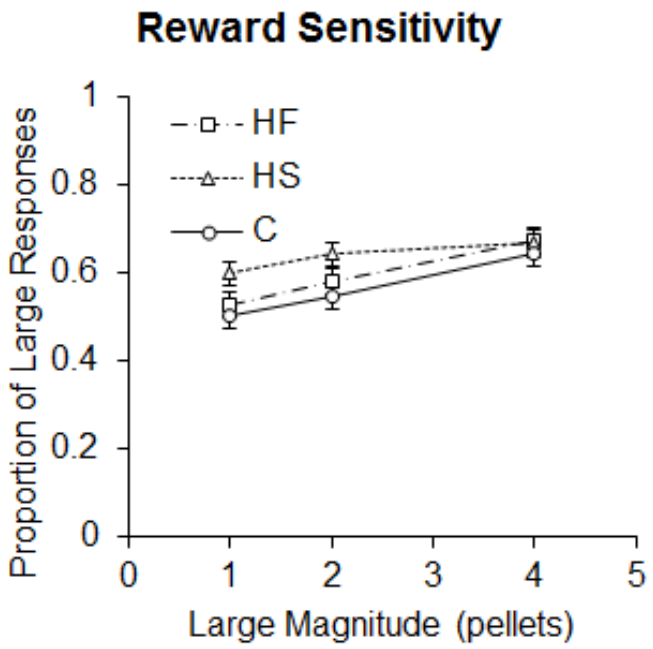


Figure 8. A) Mean (± SE of the estimates) responses per 5 mins for each pellet type during the training phase of the devaluation task. B) Mean (±SE of the estimates) responses to the devalued and nondevalued lever during the 5-min extinction test. Deval = lever that was devalued during satiation; Non = lever that was not devalued. HF = high-fat; HS = high-sugar; C = chow.

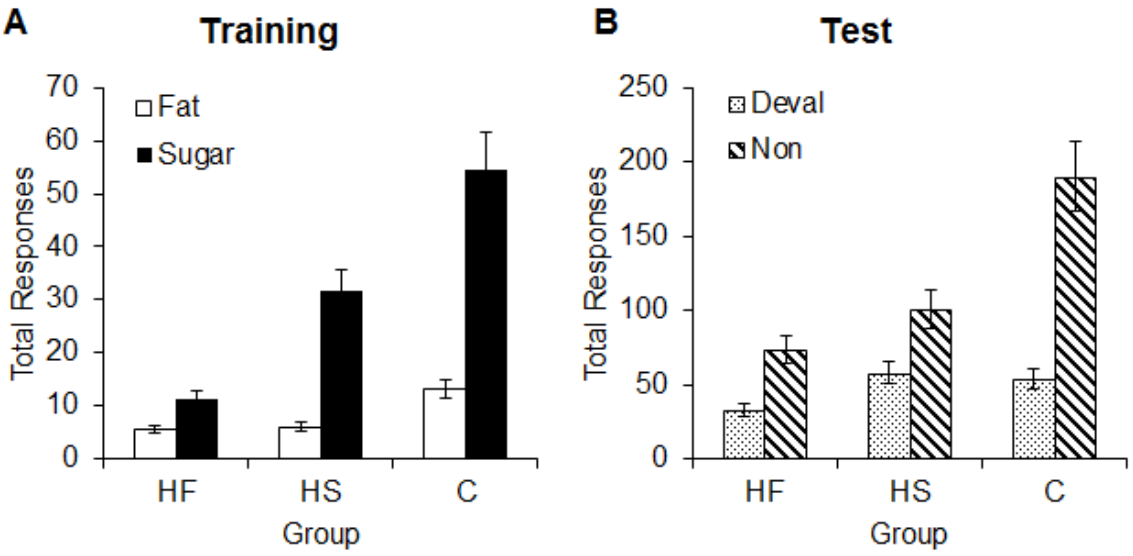
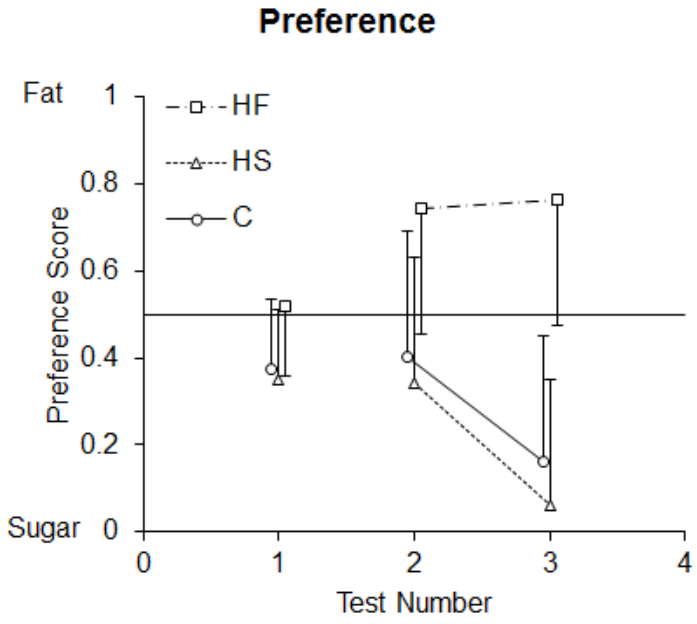


Figure 9. Mean (± SE of the estimates) preference score for each group as a function of time, where time 1 represents the exposure period and time 2 and 3 were the subsequent consumptions tests. The horizontal line represents indifference. HF = high-fat; HS = high-sugar; C = chow.



Chapter 4 - Discussion

Given that people make approximately 200 food choices a day (Wansink & Sobal, 2007) and obesity is associated with impaired decision making, the goal of the current study was to determine how long-term diet exposure affects decision making and body composition. Three aspects of decision making possibly involved in food choice were investigated: impulsive choice behavior, devaluation, and food preference. The results indicated that diets high in processed fat and sugar altered food preference and led to disruptions in impulsive choice behavior and incentive motivation, which has implications for the development of obesity and other disorders characterized by disruptions in choice behavior, such as gambling and substance abuse.

Body weight

The three behaviors measured in the current study (impulsive choice, devaluation, and food preference) have been linked to obesity. Body weight is a common measure of obesity in rodent models (Novelli et al., 2007). However, our results did not show differences in body weight following the dietary exposure. Indeed, there are inconsistent results surrounding the effect of diet on body weight, where some studies find that both high-fat and high-sugar diets lead to weight gain, while others find that only high-fat diets lead to weight gain (Jurdak & Kanarek, 2009; Jurdak et al., 2008; Steele et al., under review). The inconsistent results in weight suggest that body composition (e.g. body fat percentage) may be a better measure of obesity. In fact, the relationship between obesity and impulsive choice is more robust when using body fat percentage as a measure of obesity instead of Body Mass Index (BMI; Nederkoorn, Smulders, Havermans, Roefs, & Jansen, 2006; Rasmussen et al., 2010). In this study, there were differences in body fat percentage in the abdomen, such that the high-fat and high-sugar groups had higher body fat percentages than the chow group. Body fat percentages

were better able to detect differences in obesity resulting from diet in the present study. Schemmel, Mickelsen, and Gill (1970) proposed that body composition is under greater dietary control compared to body weight, which may explain the greater sensitivity to detect changes in body composition as a result of diet. The results suggest that high-fat and high-sugar diets can lead to higher percentages of body fat, despite controlling for the number of calories received, indicating that calorie composition has significant effects on body composition.

Impulsive choice

Impulsive choice behavior was investigated through two impulsive choice tasks to determine how changes in delay to reward and amount of reward affected the rats' willingness to wait for a larger reward. In the delay manipulation of the impulsive choice task, rats exposed to diets high in fat and sugar exhibited increased delay sensitivity, a marker of impulsivity (Odum, 2011), replicating Steele et al. (under review). While the high-fat group displayed a tendency toward a bias for immediacy, only the high-sugar diet induced a significant bias for the immediate reward. Steele et al. (under review) found that both the high-fat and high-sugar diet resulted in a bias for the immediate reward. It is possible that the effect of a high-fat diet on bias is only a modest effect, while the effect of a high-sugar diet on bias is more robust. The tendency to show a bias for the SS choice suggests that the diets, especially the high-sugar diet, are leading to suboptimal behavior compared to the chow group. Choosing the LL option was more optimal because the 60-s ITI was fixed. Therefore, even at the 5-s delay, choosing the SS would result in 1 pellet every 65 s while choosing the LL would average of 1 pellet every 45 s. The results from the delay manipulation of the impulsive choice task suggest that diets high in fat and sugar are leading to steeper discounting of delayed rewards, a marker of impulsive choice, as well as an indicator of suboptimal behavior.

The results from the time discrimination task indicated that the increased sensitivity to changes in delay exhibited by the high-fat group may be a result of poor time discrimination abilities, as the high-fat group displayed deficits in discriminating signal durations. Specifically, they had poorer temporal precision evidenced by a shallower slope of their bisection function. Poor timing abilities are predictive of increased overall impulsive choice behavior (Marshall et al., 2014). In addition, time-based behavioral interventions improve both temporal precision and impulsive choice (Smith et al., 2015). Therefore, the deficits in timing may be leading to the impulsive behavior exhibited by the high-fat group in this study and Steele et al. (under review). However, the high-sugar group did not show deficits in time discrimination, suggesting an alternative mechanism for the alterations in choice behavior. One possibility is that the high-sugar group may be exhibiting delay aversion, which is seen in individuals with ADHD (Bitsakou et al., 2009; Karalunas & Huang-Pollock, 2011). The high-sugar group did show a significant bias for immediacy which may be a marker of delay aversion. Future research should investigate delay aversion as a potential mechanism of impulsive choice for the high-sugar group.

Results from the magnitude manipulation of the impulsive choice task suggest that there were no differences in the bias for the large reward, but the rats fed a high-fat diet displayed a shallower slope suggesting they were not as sensitive to the changes in reward magnitude. The reward discrimination task further showed that the high-sugar group had a side bias, but there were no differences in the sensitivity to changes in reward magnitude. The investigation of reward discrimination does not explain the results seen in the magnitude manipulation of the impulsive choice task, as the high-fat diet did not affect reward discrimination. The relationship between reward discrimination and impulsive choice is not as robust as the relationship between

temporal discrimination and choice, as indicated by the mixed results (Marshall & Kirkpatrick, 2016; Marshall et al., 2014). However, it is possible that the mixed results are due to the nature of the tasks used to measure reward discrimination. It has been proposed that a task where the individuals behavior determines reward instead of experimental manipulations may be more sensitive to the effects of reward magnitude on behavior (Marshall & Kirkpatrick, 2016). In this study, the set experimental manipulations determined the reward (Marshall et al., 2014). It is possible that a more dynamic procedure where individuals' behavior determines reward, such as that used in Marshall and Kirkpatrick (2016), may better depict the relationship between reward discrimination and choice. Therefore, the high-fat group may have reward discrimination deficits that a more sensitive task could elucidate. Further work is needed to understand why the high-fat group showed deficits in reward sensitivity in the impulsive choice task.

Taken together, the impulsive choice and discrimination tasks show that the high-fat group showed increased delay sensitivity and poor timing precision. This suggests that poor time discrimination is likely a key factor in their deficits in impulsive choice. Although the rats fed a high-fat diet had a tendency toward exhibiting a bias for immediacy, their bias did not significantly differ from the chow group, thus showing a different pattern from Steele et al. (under review). Therefore, poor temporal precision was their dominant deficit, but they may have some modest delay tolerance issues as evidenced by an increased preference for the smaller reward at the shortest delays. However, the high-fat group also show reduced magnitude sensitivity. Results from the reward discrimination task were inconclusive suggesting that it is unclear whether the reduced magnitude sensitivity resulted from deficient reward processes, some other non-reward factor (e.g., attention, motivation, or working memory, etc.), or possibly an attentional trade-off between timing and reward processes. For example, it is possible that the

high-fat group focused attention on the delay to reward instead of the amount of reward. The high-sugar group also showed increased delay sensitivity/delay discounting, and they showed an increased bias for immediacy. Despite the deficits displayed in the delay manipulation of the impulsive choice task, the high-sugar group had relatively intact timing abilities. They also showed intact reward processing. Therefore, the deficits in impulsive choice may be a result of delay tolerance, which would affect choice behavior but not necessarily affect core timing processes.

These results provide evidence that diet induces impulsive behavior that could lead to obesity or other disorders characterized by impulsive choice. Impulsive behavior is a characteristic of many maladaptive behaviors and neurological disorders such as gambling (Alessi & Petry, 2003; Dixon et al., 2006; Dixon et al., 2003; Petry & Casarella, 1999; Reynolds, 2006), substance abuse (Bickel & Marsch, 2001; MacKillop et al., 2011; Verdejo-García et al., 2008), obesity (Bickel et al., 2014; Fields et al., 2013; Jarmolowicz et al., 2014; Rasmussen et al., 2010), and Attention Deficit Hyperactivity Disorder (ADHD; Barkley et al., 2001; Bitsakou et al., 2009; Marco et al., 2009; Neef et al., 2005). In fact, trait impulsivity is thought to predict susceptibility to disorders characterized by impulsive behavior (Velazquez-Sanchez et al., 2014; Verdejo-García et al., 2008). This diet-induced impulsivity may be a causal pathway to obesity or other disorders associated with this trans-disease process (Bickel et al., 2012). Further, these results may explain the relationship between obesity and impulsive choice that is often seen in humans (Bickel et al., 2014; Fields et al., 2013; Jarmolowicz et al., 2014; Rasmussen et al., 2010). Diet is a potential factor that may lead to obesity and impulsive behavior. Future research should investigate the causal pathways in humans and rats.

Devaluation

Devaluation was investigated to determine how diet affected the ability to update reinforcer value based on new information. Specifically, the rats were satiated on one pellet type (fat or sugar), and then were given a choice between the two pellets. The results indicated that the rats successfully devalued the reinforcer regardless of previous dietary exposure as evidenced by decreased responding to the lever associated with the pellet received during satiation. Therefore, the diets did not appear to affect habit responding or sensory-specific satiation as this would result in similar levels of responding to the devalued and non-devalued lever. These results conflict with the research investigating diet effects on devaluation. One study found that 5 weeks of exposure to sweetened condensed milk led to deficits in devaluation, such that responding was similar for the devalued and non-devalued lever (Furlong et al., 2014). Another study found that 28 days of exposure to sucrose led to deficits in devaluing reinforcers in adult rats, following three devaluation tests (Kendig et al., 2013). They proposed that diet exposure led to more habit responding (Furlong et al., 2014; Kendig et al., 2013), which does not appear to be the case in the present study. One explanation for the discrepancy may be the use of a two-lever choice paradigm in the current devaluation task as opposed to the single-lever paradigm used in previous tasks, as single-lever tasks are more likely to lead to habitual responding. In addition, in one previous study, similar responding for the devalued and non-devalued lever was not evident in rats fed sucrose diet until the third test (Kendig et al., 2013). This shift in responding occurred earlier than the chow group, which is why the authors propose they have an accelerated shift to habitual control (Kendig et al., 2013). It is possible that deficits in devaluation might have occurred in the current study if there was more extended testing. Further, another possibility is that removal from the diet before testing could affect devaluation

so that the previous studies were predominantly measuring an effect of removal from the diet. In the diet studies discussed, rats were moved to an all chow diet before testing, while rats in this study were maintained on their diets throughout experimentation. Future research should examine the effect of the current diet versus previous diet on devaluation.

The devaluation results observed in this study also suggest that sensory-specific satiety was intact in both diet groups. Further, the rats in this study responded differentially to the fat and sugar pellet indicating they were able to discriminate between the reward types. Another study showed that sensory-specific satiety was impaired in rats fed a cafeteria diet both on and off of the cafeteria diet (Reichelt et al., 2014). One possibility is that the variety in the cafeteria diet led to impairments, whereas the rats in this study were not exposed to varied diets. Another possibility is that the impairments could result from the combination of fat and sugar.

While the diets did not appear to produce a shift to habitual responding or show deficits in sensory-specific satiety, there were differences in their rate of responding in both training and testing. The high-fat and high-sugar rats responded less suggesting they did not value the reinforcers as much as the control group, illustrating potential deficits in incentive valuation. Similar results have been found in men with higher BMIs, suggesting that obesity is related to incentive valuation (Horstmann et al., 2015). Further, rats fed a cafeteria diet and rats given continuous access to sweetened condensed milk also showed fewer responses overall (Furlong et al., 2014; Reichelt et al., 2014). In our study, high-fat and high-sugar rats showed lower incentive valuation even though they successfully devalued the rewards, suggesting that long-term exposure to diet primarily affects overall incentive valuation.

Food preference

Food preferences can be innate or learned. The high-sugar and chow group showed a preference for the sugar pellets. The sugar preference displayed by the chow group is likely due to an innate preference for sugar (Sclafani, 1995). On the other hand, the rats fed a high-fat diet showed an increased preference for fat. Exposure to a particular diet can lead to strong and persistent changes in preference, depicting learned preferences (Sclafani, 1995). The results from the preference test suggest that long-term exposure to a high-fat diet overrode innate preferences, such that individuals preferred the high-fat diet that they had long-term exposure to. This has implications for humans as consumption of unhealthy foods could increase preference for those foods. However, it is critical to consider the other factors that may affect food choice behavior, as food preference is only one aspect of food choice (Mela, 2001). Specifically, incentive valuation and food preference are thought to relate to and influence food choice (Mela, 2001). Indeed, alterations of incentive valuation were found, and this could drive food choice behavior in conjunction with food preference (see Figure 1).

Conclusions

Food choices are complex, and can be influenced by a willingness to wait for reward (impulsive choice), general food preferences, and incentive valuation to seek out certain foods. Figure 1 displays the proposed connection between diet and the three factors investigated in this study and how these factors could impact on food choice and weight status/body composition. Ultimately, diet affects impulsive choice, incentive valuation, and food preferences. All three of these factors could influence food choice, and food choices determine one's diet. Finally, those food choices could contribute to weight status/body composition, as overconsumption of high-fat and high-sugar foods can lead to obesity.

It is also possible that the three factors explored in this study could influence each other. The results of this study show that rats can learn food preferences based on experience. The rats fed a high-fat diet showed a preference for fat, and this overrode the innate preference for sugar displayed by the high-sugar and chow group. This relates to incentive valuation where value is attributed to rewards based on experience (Dickinson & Balleine, 1994). Food preference and incentive valuation influence each other where hedonic responses can influence valuation and valuation of a reward affects exposure in a feedback look. Together the two represent incentive learning, where operant conditioning is driving learning. Consumption of a food item leads to rewarding effects, and then food preference is changed.

Further, food preference may be related to impulsive choice. A preference for a particular food would be expected to lead to increased consumption (Mela, 2001), which is the natural version of the dietary exposure utilized in the current study. As consumption for foods high in fat and sugar increases with increased preference (Mela, 2001), those foods would then induce increased impulsive behavior (diet-induced impulsivity), which was shown in this study and in Steele et al. (under review). In addition, impulsive behavior poses a self-control challenge in relation to food preference, where it may be difficult to wait for longer-delayed rewards, such as preparing and eating healthier foods, when the preferred foods are available sooner (e.g., fast foods).

Finally, impulsive choice and incentive valuation may be related. Indeed, incentive motivation, the willingness to work for a reward, has been implicated as a key mechanism and potential pathway to impulsive choice (Peterson, Hill, Marshall, Stuebing, & Kirkpatrick, 2015). Impairment in incentive value could lead to suboptimal choices in the impulsive choice task. Both diets led to deficits in incentive valuation, and they also showed a tendency to choose the

SS choice, indicative of suboptimal choice. The bias for immediacy, especially present in the high-sugar group, could result from alterations in incentive value. Luo, Ainslie, Giragosian, and Monterosso (2009) found that people showed greater incentive valuation for the immediate reward, despite a preference-matched delay option. This preference for the immediate reward is seen in the chow group, but the high-fat and high-sugar diets appear to exasperate the preference for the immediate reward. Therefore, alteration in incentive value for the reward could lead to suboptimal choice observed in the impulsive choice task and pose a problem for self-control. It has been proposed that self-control could help shift preference from the immediate reward (Luo et al., 2009). However, as indicated by the relationship between impulsive choice and preference, there is likely a self-control challenge. Therefore, impairments in incentive valuation could lead to a decreased willingness to wait for delayed rewards in the impulsive choice task, thus resulting in suboptimal choice. Future research should investigate how these three factors may be influencing each other to better understand how they could contribute to food choice behavior.

Together, these results suggest that diet exposure can lead to deficits in decision making that could further challenge the ability to make healthy food choices when confronted with the many food choices each day. One potential complication may be that the effects of the diets were due to micronutrient deficiencies rather than changes in the macronutrient profile of the diets. Both the high-fat and high-sugar diets replaced 40% of the daily chow ration with fat and sugar, respectively, so both groups experienced reduced micronutrient exposure compared to the control group. However, micronutrients alone are unlikely to explain the results because the high-fat and high-sugar diets produced different effects on several aspects of behavior, but both dietary groups would have experienced the same micronutrient reduction. Future research

should investigate the high-fat and high-sugar diets when micronutrients are controlled to determine if the deficits in decision making are a result of macro- and/or micro-nutrient composition.

Epstein et al. (2004) suggests that food preference dictates what one will eat and incentive motivation drives how much one will eat based on the willingness to work for reward. Impulsive choice further fits into this equation by driving whether one will wait for the reward (which could relate to waiting for healthier food options). Food preference is not enough to lead to unhealthy food choices. Rather, the individuals must be willing to work for and wait for the rewards that they prefer. Indeed, the ability to wait for the larger reward is predictive of BMI almost 40 years later, suggesting that deficits in choice behavior resulting from diet could have consequences in the future (Schlam, Wilson, Shoda, Mischel, & Ayduk, 2013).

The combined results suggest that it may be necessary to target decision making skills to help individuals combat the deficits in impulsive choice behavior and incentive valuation induced by diet, and potentially avoid the development of obesity or other maladaptive behaviors that can result from long-term consumption of foods high in processed fat and sugar. One potential avenue to improve impulsive choice behavior may be through a time-based behavioral intervention, particularly in the high-fat group which showed clear timing deficits. The high-fat diet-induced impulsivity appeared to result in poor temporal precision, and time-based interventions have successfully promoted self-controlled behavior and improved timing in rats (Smith et al., 2015). The high-sugar group may require a different intervention, as their time discrimination abilities were relatively intact. It is possible that an intervention for delay tolerance could help the high-sugar group, and this could be a target for the high-fat group as well. In addition, targeting poor incentive motivation could be a possibility for improving food

choices, as this was a hallmark effect of both diets. Future research should investigate the efficacy of interventions to determine if they could be used in treatment programs for disorders that are characterized by the trans-disease process of impulsive choice (Bickel et al., 2012).

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