ABSTRACT

D_2/D_3 RECEPTOR AGONIST, QUINPIROLE, AND HIGH FAT DIET DECREASE FAT PREFERENCE IN RATS

By Carrie J. Hass

Long term exposure to a high fat diet can cause a persistent preference for a high fat diet even after a switch to a low fat diet (Teegarden, Scott, & Bale, 2009). High fat foods stimulate the release of the neurotransmitter dopamine, which activates the reinforcing areas in the brain (Martel, & Fantino, 1996). Long term exposure to a high fat diet will decrease dopamine levels and also significantly reduce the dopamine response to a low fat food, but will still elicit a significant dopamine increase to high fat foods (Geiger et al., 2009). However, rats will significantly prefer more low than high fat foods after administration of the dopamine D_2/D_3 agonist quinpirole (Cooper, & Al-Naser, 2006). The aim of the current research was to investigate how long term exposure to a high fat diet could cause an enduring preference for high fat foods and if quinpirole could dose-dependently decrease high fat food preference.

High versus low fat food preference and total energy intake were assessed at a drug free baseline and four doses of quinpirole (0, 0.01, 0.05, 0.1 mg/kg s.c.) at two different test periods, and in each, intake was measured at 30, 60, 120 and 180 minutes. Thirteen male Sprague-Dawley rats were maintained on a high fat (HF) diet for 8 weeks (test #1) and then changed to a low fat diet for 6 weeks (test #2). Twelve rats were maintained on a low fat (LF) diet throughout the study. At test time #1 baseline, overall energy intake was lower in the HF group there were no diet group differences in fat preference. The 0.05 and 0.1 mg/kg doses decreased energy intake and fat preference in both groups. At test time #2 baseline, energy intake was similar in both groups, but the HF group had lower fat preference at 30-60 and 60-120 intervals. The 0.01, 0.05, and 0.1 mg/kg doses decreased energy intake and fat preference at test time #2 in both groups.

These results support the role of a D_2/D_3 agonist in decreasing high fat preference and have implications for the impact food preference, dietary exposure and diet maintenance on long-term eating-related health issues.

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A Thesis Submitted
In Partial Fulfillment of the Requirements
For the Degree of

Master of Science-Psychology

Experimental

at

The University of Wisconsin Oshkosh
Oshkosh, WI 54901-8621

January 2011

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To my family and friends- Thank you, thank you, thank you for all your love and support throughout this project. Especially for being so understanding when I was unable to participate in gatherings because, “I have to feed the rats.” To my parents, for always believing in me and encouraging me no matter how unusual my ideas have been. And to Eric, for always being able to make me laugh when I needed it the most. This would never have been completed without each and every one of you.

ACKNOWLEDGEMENTS

I would like to thank James Koch, PhD, my thesis chair for all his guidance and assistance throughout my thesis and my graduate school experience. Thank you also to Lee McCann, PhD and Keilah Worth, PhD for all their recommendations and criticisms of my thesis. I would also like to thank Mary Bleser, Kelly Schill, Taylor Gabourie, Tami Kuske, and Sarah Grossman for all their help with taking care of my rats.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF TABLES (Continued)

LIST OF TABLES (Continued)

LIST OF FIGURES

Introduction

Obesity is major health problem in the United States and modest weight loss by obese people will improve various health problems such as high blood pressure, high cholesterol levels and insulin resistance (Wadden et al., 2005). A common method for weight loss is dieting, which is prevalent in our society (Brownell & Rodin, 1994). However, many people find it very hard to lose weight, and commercial weight reduction programs that promote dieting have high attrition rates, ranging from 50-70% after 12 weeks (Volkmar, Stunkard, Woolston, & Bailey, 1981). This has caused some researchers to argue against dieting as a means to lose weight (Brownell & Rodin, 1994). One reported obstacle to making healthier food choices is a refusal to give up preferred foods that are typically high in fat and sugar (Morreale & Schwartz, 1995). Therefore, one possible reason for the difficulty in dieting and in losing weight is an unyielding preference for high fat foods.

High Fat Diets and Body Weight

Diets high in fat can cause obesity in animals. Barboriak, Krehl, Cowgill, and Whedon (1957) fed various groups of young, male Sprague-Dawley rats a diet of either corn oil, coconut oil, cottonseed oil, lard, butter, vegetable shortening (Crisco), or margarine over multiple experiments lasting between 6 weeks to 2 years. Lard, vegetable shortening, and butter promoted the most weight gain after two months, and it was

significantly more than the regular chow fed control group. The groups fed lard and vegetable shortening gained the most weight during the longer experiments.

Sclafani and Springer (1976) investigated the effects of dietary obesity on operant conditioning. Adult rats were either given regular chow (control group) or a cafeteria style diet (experimental group) that consisted of chow, Crisco mixed with Purina powder, sweetened condensed milk, chocolate chip cookies, salami, cheese, bananas, marshmallows, milk chocolate, and peanut butter. By the tenth day, the experimental group was significantly heavier than the control group. Rats were also trained to bar press for a chow pellet and the experimental group pressed significantly less for a pellets compared to the control group. When both groups were given only a 0.1% quinine-Purina chow diet, the experimental group adjusted poorly to the diet switch, eating significantly less food and losing significantly more weight than the control group. A follow-up experiment was conducted with male rats on an *ad libitum* supermarket diet or on a restricted supermarket diet, such that the restricted rats' weight would match rats fed only Purina chow. Adequate regular chow was available to both groups. After 20 days, a 24 hour intake of 0.1% quinine-Purina chow mash was recorded for both groups. The rats with *ad libitum* supermarket diet gained significantly more weight than the restricted rats and ate significantly less of the mash, once again demonstrating that the *ad libitum* supermarket diet contributed to the rats adjusting poorly to a lower fat diet.

Similarly, a higher fat content may lead to increased food intake such that rats will eat more of a food when the fat content is higher. Rossi, Driscoll, and Langhans (1997) fed adult rats three different levels of fat consecutively and found that rats given a

medium or high fat diet ate significantly more food compared to when they were given a low fat diet. There was also a significant increase in food intake when rats were switched from the low fat diet to the medium fat diet. The rats then ate significantly less food when they were switched from the high fat diet to the low fat diet, suggesting that they preferred the low fat diet less than the high fat diet.

Body Weight and High Fat Food Preference

The foods that children and infants consume and prefer will often predict food consumption and preference later in life, which can then impact their long-term health (Venter and Harris, 2009). Many studies with humans have found positive correlations between a high fat food preference and increased body weight. Ricketts (1997) investigated fat preference, fat intake, body composition and body mass index (BMI) in 88 elementary school children aged 9-12 years. Food intake was assessed by a three-day diet record maintained by the children, along with help from parents. Body composition was assessed by height and weight, as well as triceps and subscapular skinfolds. The fat preference test had participants rate high and low fat versions of brownies, peanut butter cookies, chocolate cake, and chocolate chip cookies. A significant positive correlation existed between high fat food preference and high fat intake. High fat food preference also showed a significant positive correlation with triceps skinfold measurements and BMI.

Similar correlations have been found in adults. One questionnaire found that overweight subjects consumed significantly more fresh and processed meats, frozen dairy

desserts, pastries, and snacks such as potato chips compared to underweight subjects (Pangborn, Bos, & Stern, 1985). In another study, 30 adults rated their fat preference of 10 foods that were prepared with two to five different levels of fat content. There was a significant positive correlation between the percentage of body fat and the overall preference for the higher level of fat content (Mela & Sacchetti, 1991).

The preference for foods high in fat does not necessarily indicate a preference for foods high in sugar. Drewnowski, Brunzell, Sande, Iverius, and Greenwood (1985) found that increased BMI was significantly correlated with preference for a high fat and low sugar mixture of milk, cream, and sugar. However, normal weight participants preferred a mixture that was high in sugar and low in fat, and formerly obese participants preferred a mixture that was high in both sugar and fat.

One study examined environmental influences on the dietary fat preferences of 23 pairs of monozygotic twins, (Rissanen et al., 2002). The twins were raised in the same house, however one twin developed a BMI that classified them as obese and the other was normal weight (lean). The average BMI difference was 7 kg/m^2 after living apart for an average of 25 years. When recalling eating habits from the time when they moved away from each other, the obese twin recalled eating significantly more food in general and consuming significantly more high fat foods and alcoholic beverages than the lean twin. Current food preference and eating habits showed the obese twin reported a significantly greater preference for high fat foods than the lean twin, and neither twin showed a preference for sweet foods. The obese twin also reported a significantly greater tendency to overeat in one sitting compared to the lean twin, and this overconsumption

consisted of a preference for sandwiches/pastries/pies, ice cream/desserts, and alcoholic beverages. These results suggest that preference for and increased consumption of dietary fat has an environmental component that may promote the development of obesity.

High Fat Food Preference

Food preferences can be acquired over time and result from genetic predispositions interacting with the environment (Birch, 1999). Birch defines preference as, "the selection of one item over others … (and) connotes that liking is the basis for selection, although liking is only one of a number of motives that affect food selection," (p.42). Specific food preferences develop through familiarity with and consumption of a specific food, which emphasizes that availability and accessibility can determine a food preference. Foods that are high in fat are readily available and inexpensive in the United States (Hill & Peters, 1998). Hence, the current environment may contribute to a preference for foods high in fat.

The environment can also affect food preference though conditioning. A preference for flavors with high dietary fat was conditioned in children 2-5 years old (Johnson, McPhee, & Birch, 1991). Children consumed two different flavored yogurts, one high fat and one low fat, over 8 sessions. Preference for the flavor associated with high dietary fat significantly increased by the eighth session, while preference for the flavor paired with low dietary fat stayed the same.

A follow-up conditioning study was conducted with children 3-4 years old (Kern, McPhee, Fisher, Johnson, & Birch, 1993). Children were given two different flavors of a

high fat or fat free yogurt on consecutive days, once a week for 6 weeks. Children significantly preferred the flavor of the high fat yogurt compared to their baseline preference rating as well as preference for the fat free flavor, while preference for the fat free flavor did not change. The significant preference for the high fat flavor compared to the baseline preference rating persisted for two months afterwards. However, there was no longer a significant difference between the preference for the high fat and fat free flavor, and preference for the fat free flavor remained the same. Thus, a persisting preference for high fat foods can develop because of familiarity and consumption.

Early exposure to a specific type of diet can establish a preference for the same diet later in life. Warwick, Schiffman, and Anderson (1990) found that rats initially given a high fat diet for 4 weeks will significantly prefer a higher fat food during a preference test compared to rats that were initially fed a low fat diet. Two groups of female Sprague-Dawley rats (21-23 days old) were first given either a high (30% of calories) or a low fat (10% of calories) diet for 4 weeks. Following 5 hours of food and water deprivation, rats were then presented with a low fat option of plain peanut butter, a medium fat option of peanut butter with 21% peanut oil added, and a high fat option of peanut butter with 41% peanut oil added for two hours. This dietary fat preference test was conducted for five consecutive days. There were no significant differences in intake or fat preference between the groups. Following this, half of the rats from both groups switched diets for the second phase of the study and were maintained on this diet for 4 weeks. The diet switch did not produce significant intake differences between the groups during the dietary fat preference tests. The groups were collapsed by the first phase diet and were

designated as low fat (low fat/low fat and low fat/high fat) and high fat (high fat/high fat and high fat/low fat). Body weights were not significantly different between groups. The high fat group consumed significantly more total fat and more of the high fat option of peanut butter over all five test sessions compared to the low fat group. All rats significantly preferred a fat content similar to their initial diet, whether it was high or low fat. The authors note that the preference may be due to the young age of the rats, but it is notable that the preference was maintained even after a diet switch for half of the rats.

The persisting high fat preference has also been shown by Teegarden, Scott, and Bale (2009) who investigated the effects of a high fat diet on young mice. Three week old mice consumed a high fat diet while control mice consumed standard chow for one week. All mice then consumed standard chow. The mice then completed a 10 day preference test at three months of age and the mice pre-exposed to a high fat diet significantly preferred the high fat diet compared to the control group that preferred the high carbohydrate diet.

A similar preference has been shown to develop in adult rats. A study by Reed, Friedman, and Tordoff (1992) investigated the effects of a high fat, high carbohydrate, or high protein diet, as well as regular chow on subsequent macronutrient preference. Rats were assigned to the different diets along with access to chow for four days. Chow was then discontinued and only the high fat, high carbohydrate, and high protein diets were offered for 12 days. All rats were then switched to only chow for 34 days, which was followed by a two day macronutrient preference test for 2 days. A second experiment offered the macronutrients along with chow for 4 days, followed by only chow for 5

days, and then only macronutrients for 4 days. The rats in the high fat and high carbohydrate group ingested significantly more calories and preferred their original macronutrient diet in both macronutrient preference tests. Rats that were only exposed to chow did not significantly prefer a macronutrient.

Maintenance of a preference for high fat foods despite a dietary change also exists in humans. Mattes (1993) investigated the effects of fat preference in healthy adults by assigning diet groups such that they could not eat fat (ND fat), they could eat only fat-modified products in moderation (M-Fat), or no change to diet (control). Twenty-seven participants adhered to the diet for 12 weeks and then were allowed to eat whatever they desired for 12 weeks. All participants had monthly meetings where they completed a food preference questionnaire. Both ND and M-Fat groups significantly reduced their fat intake only during the diet period and returned to their baseline fat intake during the follow-up period.

However, some studies with humans have shown that switching to a low fat diet may alter food preference, possibly because of frequent social reinforcement. A study by Grieve and Vander Weg (2003) found that when obese women followed a diet lower in fat than their usual diet for 12 weeks, they reduced their desire and consumption of high fat foods and increased their desire for low fat foods. They did not differ in actual consumption of low fat foods or in their desire or consumption of medium fat foods and drinks. The authors suggest that the weekly meetings may have socially reinforced the low fat diet, rather than the diet change alone.

In summary, animals maintained on a high fat diet will significantly consume more high fat foods than low fat foods compared to animals maintained on a low fat diet, and a high fat diet has been shown to cause obesity. A preference for a high fat diet is correlated with increased body weight and food preferences can be conditioned and develop through familiarity and consumption. Additionally, preference for a high fat diet will persist even after a diet change to a low fat diet. The question remains if there is a neurochemical component contributing to why people and animals continue to prefer and eat high fat food past a healthy body weight.

Ingestion and Dopamine

Food ingestion is a complex process that involves a number of biological (including neurochemical), cognitive, environmental, emotional, economic, and sociocultural factors (Drewnowski, 1997). Behavioral methods used in ingestion research include operant conditioning (lever pressing) and intracranial self-stimulation. Detection of neurotransmitters, receptors, and neuronal activity occurs via microdialysis, histological techniques, and imaging the brain, such as with autoradiography or positron emission tomography (PET). Additionally, behavioral pharmacology research in ingestion involves measuring the effects of drug administration on intake amounts and patterns alone or in combination with the methods listed above. The studies presented below use one or more of these techniques.

The current research focuses on a possible neurochemical influence for an enduring fat preference as described above. Ingestion is modulated or mediated by

several brain neurotransmitters and neuropeptides, including dopamine, noradrenaline, and serotonin (Schwartz, Woods, Porte Jr, Seeley, & Baskin, 2000). Dopamine specifically has been implicated for its role not only in food ingestion, but also movement, reward, and reinforcement of behaviors necessary for life. Dopamine synthesis begins with the amino acid tyrosine that is oxidized by the enzyme tyrosine hydroxylase and becomes L-Dopa, which is then transformed by dopa decarboxylase into dopamine (for review see Fuxe et al., 1985). The dopamine transporter (DAT) regulates synaptic dopamine concentration by controlling the reuptake of the neurotransmitter back into the presynaptic terminals following release. When levels of synaptic dopamine are low, the levels of DAT will decrease so that levels of synaptic dopamine are able to increase back to baseline and homeostasis can be maintained (South & Huang, 2008).

Dopamine is distributed by several major pathways in the brain. The mesolimbic system originates in the ventral tegemental area (VTA) in the midbrain, and receives signals from the ventral striatum and the hypothalamus, areas also implicated in control of ingestion. During VTA activation, there is an increase in the release of the dopamine into the nucleus accumbens (NAc), amygdala, and hippocampus (Fuxe et al., 1985; Palmiter, 2007). Di Chiara and Bassareo (2007) explain that the NAc is located in the ventral striatum and is divided into an inner core and an outer shell, and the latter has been highlighted as the most sensitive site for dopamine-dependent reward. A second dopamine system, the nigrostriatal originates in the substantia nigra (SN) and projects to the dorsal striatum, which is often referred to as caudate-putamen (CP). This system is mainly associated with movement control (Palmiter, 2007). A third dopamine system, the

mesocorticolimbic, originates in the VTA and SN and projects mainly to the prefrontal cortex, hippocampus, and amygdala and modulates positive reinforcement (Fuxe et al., 1985).

Research has linked food ingestion to the mesolimbic system, which is also referred to as the reward system in the brain (Hernandez & Hoebel, 1988). The reinforcing effects of the mesolimbic system were initially discovered when rats with electrodes implanted in their septal area, would frequently and for extended periods of time press a lever to self-stimulate (Olds, & Milner, 1954). It was later discovered that rats found self-stimulation of the hypothalamus the most intensely rewarding (Olds, Travis, & Schwing, 1960). The hypothalamus sends initial signals to the mesolimbic system in which dopamine is then released in response to an important stimulus and increases the amount of attention a person will give to the stimulus (Palmiter, 2007). Currently, there exist four possibilities for how the reward system actually works. It either is associated with the pleasure of sex, drugs and food (hedonic), the activation of the sensorimotor system (vigilance), the association of cues that bring the reward (learning), or it motivates the response action to a specific environmental stimulus (appetitive) (Berridge, 2007). Regardless, dopamine and the mesolimbic system are implicated in rewarding behaviors and there is likely overlap among the four theories of its mechanism of action.

Several studies have used microdialysis (collection of extracellular fluid) to measure the levels of dopamine and its metabolites, dihydroxyphenylcetic acid (DOPAC), and homovanillic acid (HVA) during eating. Levels of all three significantly

increase in the NAc in response to eating chow (Hernandez & Hoebel, 1988). These increased levels outlast the actual consumption, suggesting another purpose for the increased dopamine beyond the act of consumption itself.

High Fat Food and Dopamine

Interestingly, eating a palatable food increases the extracellular levels of dopamine more than eating regular chow in rats. Martel and Fantino (1996a) monitored the amount of dopamine and its metabolites, DOPAC and HVA, in the NAc shell during feeding of a high (short cakes) and low (regular chow) palatable food in rats. The rats ate significantly more high than low palatable food. Dopamine levels were significantly higher while the rats ate high and low palatable food compared to baseline, and they were significantly higher when the rats ate the high compared to the low palatable food. Also, the metabolites' levels were significantly higher while the rats ate the high compared to the low palatable food and baseline.

Martel and Fantino (1996b) then measured levels of dopamine and metabolites released in the NAc in response to the amount of high palatable food. Rats were presented with an unrestricted amount of short cakes on the first day, followed by a restricted amount on the second day, and absence of food on the third day. Dopamine levels were significantly higher in the unrestricted feeding compared to all other conditions. With the restricted amount, dopamine levels were significantly higher than in the absence of food, but were not significantly higher than baseline. Dopamine levels decreased in the absence of food, but not significantly below baseline, and DOPAC and

HVA levels rose significantly only in the unrestricted condition. Thus, prolonged exposure to a palatable food increases dopamine release in the mesolimbic pathway more than both a low palatable food or brief exposure to a high palatable food.

Bassareo and Di Chiara (1997) investigated the influence of a novel food on extracellular dopamine release in the medial prefrontal cortex and in the medial NAc. Male Sprague-Dawley rats were maintained on standard chow but were also fed the novel food Fonzies, an Italian version of Cheetos®, which is made with corn flour and vegetable fat. The first experiment found that during Fonzies exposure, rats released significantly higher levels of dopamine in the prefrontal cortex and the NAc compared to their baseline values. Also, rats with previous Fonzies exposure had significantly lower levels of dopamine in the NAc compared to Fonzies-naïve rats. The second experiment found a significant reduction in the NAc dopamine levels during the second presentation of Fonzies compared to the first, but not in the prefrontal cortex. This is suggestive of habituation to the feeding-induced stimulation of dopamine transmission in the NAc after a Fonzies meal and the third experiment investigated the recovery from this habituation. Rats were divided into three groups: exposure 5 days prior, one day prior, or no exposure (Fonzies-naïve). The two groups previously exposed to Fonzies had a significantly shorter latency to eat after Fonzies were presented and ate significantly more than the Fonzies-naïve group. Both the Fonzies-naïve and the 5 day prior group had a significantly higher level of dopamine release in NAc compared to the 1 day prior group and baseline. The 5 day prior group also had significantly higher levels of dopamine than the Fonzies-naïve group. All groups had significantly higher levels of dopamine in the prefrontal

cortex and NAc in response to the Fonzies feeding compared to baseline. Overall, there appears to be an initial surge in dopamine release in response to a novel food, but repeated exposure can reduce the levels of dopamine in the extracellular fluid. However, after five days of non-exposure the levels of dopamine will rebound and will even exceed those in rats naïve to the novel food. This indicates that dopamine can begin to return to normal levels after only five days.

Long term exposure to a high fat diet is associated with decreased dopamine activity. Levin, Triscari, and Sullivan (1986) fed rats a high fat diet for three months and found a significantly lower rate of dopamine turnover in the ventromedial hypothalamic nucleus, the dorsomedial nucleus, and the median eminence of the hypothalamus, areas that are important in ingestion.

Davis et al. (2008) investigated the effects of rats being fed either a high or low fat diet on dopamine levels in the mesolimbic system and in a sucrose reinforcement operant conditioning paradigm. For 12 weeks, the experimenters fed rats a high fat diet (HF), a standard chow diet (SC) or a restricted amount of the high diet (PF) to keep them at the same weight as the SC rats. The HF group was significantly heavier than the SC and PF groups and had comparatively lower response rates for the fixed ratio task. Additionally, the HF and PF groups both had decreased progressive ratio operant response rates compared to the SC group. The high fat diet, regardless of weight differences between the HF and PF groups, appeared responsible for the decreased response rate for a sucrose reward. Finally, rats in the HF and PF groups had significantly lower levels of dopamine turnover in the NAc compared to the SC group.

Geiger et al. (2009) examined how dietary obesity affected dopamine neurotransmission in the NAc. The authors posited that an overabundance of rewarding palatable food can lead to increased body weight which the homeostatic mechanisms responsible for body weight regulation are unable to overcome. For 15 weeks, female Sprague-Dawley rats were fed either lab chow (control) or the cafeteria style diet (DIO) previously described (Sclafani & Springer, 1976). The DIO group preferred the sweetened condensed milk and sugar water, and they consumed significantly less chow than the control group. They also gained significantly more weight than the control group, 444g and 344g respectively. In week 14, microdialysis cannulae were inserted. The DIO group had significantly lower levels of extracellular dopamine, and its metabolites, HVA and DOPAC, in the NAc compared to the control group. The DIO group also had significantly lower levels of dopamine in the NAc and dorsal striatum (or CP) compared to the control group in response to electrical stimulation. In response to a meal of lab chow, the dopamine levels significantly increased in the control group compared to the DIO group. However, levels of dopamine and DOPAC significantly increased in DIO in response to the cafeteria style diet compared to baseline. Thus, long term exposure to a high fat diet caused significantly lower levels of dopamine and its metabolites in the mesolimbic system. The exposure to a high fat diet also caused a significant reduction in dopamine release in response to chow compared to a group maintained on a low fat diet, which may suggest that they no longer found chow to be reinforcing. But there was a significant dopamine increase in response to a high fat diet compared to baseline, which implies the high fat diet is reinforcing. A closer

investigation of the dopamine receptors involved may reveal a possible pharmaceutical intervention that could counter the effects of a high fat diet.

Dopamine receptors are located pre-and post-synaptically, and there are five receptor subtypes (D_1, D_2, D_3, D_4, D_5). They are divided into two groups: D_1- like which consists of D_1 and D_5, and D_2- like which consists of D_2, D_3 and D_4 (Missale, Nash, Robinson, Jaber, & Caron, 1998). The receptor groups have a similar genetic structure which allows for some drugs to have an affinity for multiple receptor subtypes within a group. The D_1, D_2, and D_3 receptors are the main focus of the current research. D_1 receptors are located in the NAc, striatum, hypothalamus, thalamus, and limbic system. D_2 receptors are in the core of the NAc, striatum, hypothalamus, SN and the VTA. D_3 receptors are located in the NAc shell, VTA, and SN, along with a sparse amount located in the striatum. Past animal research with drug self-administration has shown that D_1 and D_2 receptors play a prominent role in reinforcing behaviors. D_2 receptor activation is involved with the incentive to seek drug reward, while D_1 receptor activation reduces drug reward seeking behavior. The D_3 receptor may also decrease drug reward seeking behavior by enhancing the effects of the previously administered drug.

Other research has used dopamine agonists, or drugs that facilitate the effects of dopamine at specific receptors, to investigate the dopamine D_1, D_2, and D_3 receptors in the NAc and their role in rewarding behavior (Ikemoto, Glazier, Murphy, & McBride, 1997). Rats were able to self-administer the dopamine D_1 agonist, SKF 38393, and the dopamine D_2/D_3 agonist, quinpirole, into the shell or core of the NAc. Rats indicated a rewarding effect by self-administering a mixture of both SKF 38393 and quinpirole into

the shell. This implies that dopamine D_1, D_2, and D_3 receptors in the NAc shell are integral to reinforcing rewards.

Wang et al. (2001) used positron emission tomography (PET) to assess dopamine receptor availability in obese people. Participants were scanned after they received raclopride (a radiotracer that binds to D_2 receptors) to measure the amount of brain dopamine D_2 receptors and after they received 2-deoxy-2 fluoro-D-glucose to measure brain metabolism. Significantly lower dopamine D_2 receptor availability was found in the striatum of obese participants compared to normal weight controls. Interestingly, the levels of dopamine D_2 receptor availability were negatively correlated with BMI. The obese participants and controls did not differ on overall brain metabolism.

Decreased levels of dopamine D_2 receptors were also found in animals. Huang et al. (2006) used the C57B1/6 breed of mice that are either prone or resistant to developing obesity when maintained on a high fat diet. They were fed a high fat diet for 20 weeks and a group of control mice were fed chow. Afterwards, brains were analyzed by autoradiography for levels of mRNA expression of D_2 receptors. The obesity-prone mice had significantly lower levels of D_2 receptors in the CP compared to the obesity- resistant and control mice. The obesity-prone mice ate significantly more food and weighed significantly more than the obesity-resistant and control mice. The decrease D_2 receptor levels in obesity-prone mice is similar to the results from the study by Wang et al. (2001).

The effect of a high fat diet and subsequent diet change on the levels of dopamine D_2 receptors and DAT in the NAc and CP were investigated by South and Huang (2008). Male mice were fed a high fat (HF) and a low fat diet (LF) for 20 days. Mice from both

groups were sacrificed, and the remaining HF group was switched to the low fat diet and sacrificed after one (HF+1) or seven days (HF+7). After 20 days, the HF and LF group consumed the same amount of food. However, after the diet switch the HF+1 and HF+7 groups consumed significantly less food than the HF group. All three HF groups weighed significantly more than the LF group.

Autoradiography showed the HF and HF+1 groups had significantly higher D_2 receptor levels in the dorsocaudal CP, ventrocaudal CP, and NAc compared to the LF group. The levels of D_2 receptors did not significantly differ between the HF+7 and LF groups. The HF group had significantly lower levels of DAT in the dorsocaudal CP and ventrocaudal CP than the LF group. Also, the HF+1 and HF+7 groups had significantly lower levels of DAT in the dorsocaudal CP, ventrocaudal CP, and NAc shell compared to the LF group. Also, final body weight was negatively correlated with level of DAT in the NAc shell and CP and positively correlated with the level of dopamine D_2 receptors.

These results are in agreement with past research which shows synaptic dopamine shares an inverse relationship with D_2 levels and a positive relationship with DAT. Therefore, higher D_2 levels and lower DAT levels are suggestive of a high fat diet causing lower synaptic dopamine activity and this may be a compensatory effort to drive synaptic dopamine levels back to homeostasis. Interestingly, the levels of dopamine D_2 receptors decreased after 7 days of a low fat diet to match those of the LF group, which suggests that dopamine levels were regulating back to pre-high fat diet levels.

Li et al. (2009) investigated the effects of a high fat diet on the expression of tyrosine hydroxylase (dopamine precursor) mRNA in three different brain regions in

mice. This study also used the C57B1/6 breed of mice that will either become obese (DIO) or stay lean (DR) on a high fat diet. All mice were fed a high fat diet for 8 weeks, during which the DIO group gained significantly more weight. The mice were then divided and either given a high fat diet (DIO-H and DR-H), a low fat diet (DIO-L and DR-L), and or a restricted amount of high fat diet (DIO-P and DR-P) for six more weeks. Both high fat groups continued to gain weight and were significantly heavier than their 8 week weight. The low fat groups maintained their 8 week weight, while both restricted groups lost a significant amount of weight compared to their 8 week weight. The DIO-H ate significantly more food than the DR-H rats and the DIO-L group ate significantly more food than the DR-L rats.

The experimenters also investigated the involvement of dopamine in the VTA, SN, and the ventromedial hypothalamus (VMH). In all three areas, the level of tyrosine hydroxylase mRNA expression was significantly lower in the groups maintained on a high fat diet (DIO-H, DR-H, DIO-P, and DR-P) compared to a group of control mice that were fed low fat chow the entire experiment. After six weeks of low fat diet switch, the DR-L group had significantly higher levels of tyrosine hydroxylase mRNA expression in the VMH and the VTA compared to the DR-H group that stayed on a high fat diet. The DIO-L group also had a significantly higher level of tyrosine hydroxylase mRNA expression in the SN compared to the DIO-H group. These results show that levels of tyrosine hydroxylase mRNA expression can be altered by diet rather than weight.

Dopamine Agonists and Ingestion

Based on the above results, high fat diets will decrease dopamine levels in the brain but switching to a low fat diet can start to reverse these changes, even after only six weeks. A possible pharmaceutical intervention to assist in attenuating the consumption of high fat foods would be a medication that increases dopamine levels in the brain. Past research by Goldfield, Lorello, and Doucet (2007) showed that methylphenidate (MPH), a dopamine transport or uptake inhibitor, given prior to meal reduced overall calorie intake and fat intake by 17% in humans. The researchers recruited 7 male and 7 female participants with a BMI over 20. All participants fasted for 12 hours prior to arriving at the lab in the morning, and there were two testing sessions, one with a placebo and one with 0.5mg MPH. Participants were allowed to eat to satiation at a buffet style lunch, where unbeknownst to the participant, the food was weighed before and after. Participants ate significantly fewer calories and significantly less fat when given MPH compared to a placebo. There were no differences in carbohydrate or protein intakes between the two groups. MPH also lessened the premeal hunger rating compared to placebo. However, it is still unknown if MPH may also affect other neurotransmitters involved with ingestion, such as norepinenphrine and serotonin (Wilens, 2008).

Another study by McQuade, Benoit, Woods, and Seeley (2003) examined how a D_2/D_3 agonist, 7-OH-DPAT, affected feeding behavior. In the first experiment, male Long Evans rats had free access to either chow or high fat diet for one month. 7-OH-DPAT was administered by subcutaneous injection in 0 (vehicle), 10 (low), 50 (medium), and 100 (high) µg/kg doses (within subjects for all experiments). Food was removed 2

hours prior to injection and then given back 15 minutes post injection with intake monitored for 3 hours (at 30, 60, and 180 minutes). All doses significantly reduced food intake compared to vehicle for both high fat and chow groups.

In the second experiment, rats had 3 hours of access to either chow or high fat diet each day for 3 weeks. A subcutaneous injection of 7-OH-DPAT was administered 15 minutes prior to feeding in the same doses. The high fat group ate significantly more than the chow group when given vehicle and high dose, except the high dose did significantly reduce feeding at only 180 minutes. Intake was significantly reduced for the high fat and chow groups with both the medium and high doses compared to vehicle.

Rats in the third experiment had *ad libitum* access to chow or a high fat diet, and then they were food deprived for 21 hours once a week for 2 weeks. Following deprivation, vehicle, low, and the medium dose of 7-OH-DPAT was administered (within subjects) prior to food presentation, and intake was monitored. None of the doses reduced intake of chow, but the medium dose significantly reduced intake of high fat food at 30 minutes and both doses significantly reduced intake of high fat food at 60 minutes compared to vehicle. Overall, a D_2/D_3 agonist produced a dose-dependent decrease in the consumption of a high fat diet, despite the rats being maintained on the diet for a few weeks.

Quinpirole is a D_2/D_3 agonist that produces a rewarding effect in the NAc in rats (Ikemoto et al., 1997). Quinpirole is very similar to7-OH-DPAT in that they have a similar binding affinity for D_2/D_3 receptors (Missale et al., 1998).

Quinpirole is effective at decreasing operant responding for food. Hoffman and Beninger (1989) trained rats to lever press for food on a variable schedule. After responding stabilized, rats were injected with quinpirole (0.01, 0.1, 1.0 mg/kg intraperitoneal) and immediately placed in the operant chamber. Quinpirole produced a significant dose-dependent decline in overall response rates compared to a vehicle during the 30 minute sessions.

A study by Kaur and Kulkarni (2002) investigated the effects of various D_1 and D_2 agonists and antagonists on different feeding behaviors. One behavior was the hyperphagia that is caused by atypical antipsychotics, such as clozapine. Mice were maintained on regular chow and food deprived one hour prior to testing. They were then given an intraperitoneal injection of quinpirole (0.0125, 0.025, or 0.05 mg/kg) and after 45 minutes were allowed to free feed on chow mixed with sucrose. The 0.0125 dose significantly decreased food intake at 0.5, 1, 2, and 4 hours compared to control. Also, all three doses reversed the clozapine-induced hyperphagia at the 0.5, 1, 2, 3, and 4 hour time intervals.

Quinpirole also decreases consumption of a palatable high fat food. Cooper and Al-Naser (2006) investigated the behavioral effects of quinpirole on food preference in food-deprived rats. For ten days, male hooded rats were food-deprived for 22 hours a day. Following three familiarization trials on consecutive days, the rats were given a choice between a high-palatable, high-fat, high-sugar food (chocolate-coated biscuits) and a low-palatable food (regular maintenance diet). The rats were administered quinpirole (0.03, 0.1, 0.3 mg/kg, subcutaneous) 30 minutes prior to the test (between

subjects). During the 15 minute test, food intake was monitored and rats were observed for: 1) eating food pellets 2) eating chocolate biscuits 3) locomotor activity 4) rearing 5) grooming 6) oral responses-yawning, chewing, licking, biting containers 7) immobility.

Quinpirole produced significant dose-dependent decreases in the total amount of food consumed, and the rats ate less high-palatable food and more low-palatable food (0.03 and 0.1). Quinpirole also completely suppressed grooming at the higher doses (0.1 and 0.3). The authors noted that quinpirole did not interfere with the initiation of feeding, however, it did reduce the amount of time spent eating the high palatable food.

In review, animals maintained on a high fat diet will gain a significant amount of body weight and consume significantly more high fat foods than low fat foods compared to animals maintained on a low fat diet. Increased body weight is correlated with a preference for a high fat diet. Food preferences can develop through familiarity and consumption and can also be conditioned. A significant preference for high fat foods will continue even after a diet change to a low fat diet. A possible factor in this persisting preference is dopamine levels, whose fluctuations impact ingestion and reward. Dopamine levels immediately increase in response to food and will significantly increase even more in response to high fat foods. However, long term exposure to high fat foods will cause a significant decrease in levels of extracellular dopamine, its metabolites, and receptors. The long term exposure in animals also significantly reduces the dopamine response (increase) to a low fat food, but will still elicit a significant dopamine increase to high fat foods. Some studies have shown that these levels will start to rebound with a change to a low fat diet. Dopamine agonists decrease eating of low and high fat foods.

Specifically, quinpirole, a dopamine D_2/D_3 agonist decreases overall consumption of food and the preference for a palatable food.

Previous studies have used multitude of high fat diets such as the cafeteria style diet, high fat pellets with added sugar, and chow mixtures with different amounts of added safflower oil. The current experiment maintained rats on a high fat diet which consisted of adding fat (and calories) to regular chow, so that the only nutritive manipulation was amount of fat content, without other additives such as sugar. This was to investigate differences in high and low fat diet preference and body weight of rats maintained on a high versus low fat diet for 8 weeks. Test time #1 included a 24 hour intake test, familiarization trials, baseline #1, and drug tests #1. During the drug tests, the rats were given varying doses of quinpirole and differences in food preferences were assessed again. All rats were then maintained on a low fat diet for 6 weeks, and dietary preferences were again assessed alone and with varying doses of quinpirole (test time #2). Despite the proven efficacy of quinpirole in decreasing feeding of regular chow and palatable food in rodents, it has not been used as a pharmaceutical intervention in a long term dietary manipulation study. The overall goal of this experiment was to investigate the impact of environmental influences (dietary fat composition) on one factor of ingestion (fat preference) and its interaction with one of the major brain neurotransmitters, dopamine. Results of this research could be used to further knowledge on appetite control for weight loss, by both modifying dietary choices and utilizing pharmaceuticals that are similar to quinpirole.

Hypotheses

Hypothesis 1:

The different diets will cause a significant difference in body weights between the HF group and the LF group at baseline #1.

Hypothesis 2:

At baseline preference test times #1 and #2, rats in the HF group will have a significantly greater total energy intake and preference for high fat food than rats in the LF group.

Hypothesis 3:

At test times #1 and #2, quinpirole will produce a significant dose-dependent decrease in overall energy intake in both diet groups.

Hypothesis 4:

At test times #1 and #2, quinpirole will produce a significant dose-dependent decrease in overall high fat food preference in the HF group.

Hypothesis 5:

The dose-dependent effects of quinpirole on high fat food preference will be significantly less at test time #2 versus test time #1 in the HF group as compared to the LF group.

Methods

Subjects

Twenty-five male Sprague Dawley rats (Harlan, U.S.A.) were individually housed in polycarbonate shoe box cages with contact bedding and a wire mesh top (26 x 48 x 20 cm h), in a temperature controlled room (21º C). Rats were moved to aluminum cages with a wire mesh bottom (21 x 28 x 19 cm h) for familiarization and testing, which is described below. Both sets of cages contained a 14 cm long and 7.5 cm in diameter PVC pipe. The room was maintained under a reverse 12 hour light/dark cycle (lights off at 12:00 h) with red light illumination during the dark cycle. At 9 weeks of age, the rats were divided into two initially weight-matched groups and were fed either a high or low fat diet, which is described below. Water was available *ad libitum* throughout the study and preference tests. Body weight was monitored 2-3 times per week. All procedures were approved by the University of Wisconsin-Oshkosh Institutional Animal Care and Use Committee.

Materials

Food

Rats were given *ad libitum* access to either a low or high fat diet, except prior to and during the food preference tests as described below. The low fat diet was standard laboratory chow pellets (Harlan Tekland Rodent Diet 8604 W, Laboratory Diets Inc.). The high fat diet was two parts ground chow and one part melted vegetable shortening

(Crisco® All-Vegetable Shortening) that was mixed thoroughly while still hot, allowed to cool and then remixed. It was stored at room temperature and prepared fresh every third day or as necessary (Wellman, Nation, & Davis, 2007). The low fat diet contained 4.5% fat and 24.8% protein by weight, and has an energy content of 3.3 kcal/g. The high fat diet contained approximately 35.9% fat and 16.3% protein by weight, and had an energy content of 5.3 kcal/g. Each diet was presented in a single round, glass jar (spring-clipped to the inside of the cage) with a height of 6.5 cm and a diameter of 5cm.

Drug

The D2/D3 agonist (-)-Quinpirole hydrochloride was purchased from Sigma Aldrich (St. Louis) and dissolved in distilled water (vehicle).

Procedure

Food schedule

Thirteen rats were fed a high fat (HF group) diet and twelve rats were fed a low fat (LF group) diet for 8 weeks (weeks 1-8) and throughout the food preference testing time #1 (see description below) which occurred during weeks 9 and 10. HF rats were then switched to the same *ad libitum* low fat diet as the LF rats, and both groups were fed the low fat diet for an additional 6 weeks (weeks 11-16). Food preference testing time #2 occurred during weeks 17 and 18 (see Table 1 for schedule).

Quinpirole administration

Quinpirole was injected subcutaneously (s.c.) at doses of 0 (vehicle), 0.01 (low), 0.05 (medium), and 0.1 (high) mg/kg at an injection volume of 1 ml/kg, for a total of 4

injections per rat at each of the two test times. Doses were counterbalanced to avoid order effects. All injections were freshly prepared and administered 30 minutes prior to lights out. The HF and LF groups were tested on alternate days with an extra day in between, so that there were 72 hours between injections.

Food preference tests

During weeks 8 and 16, two 24 hour food intake tests were conducted to acclimate the rats to the aluminum testing cages. During weeks 9 and 17, three familiarization trials took place on three consecutive days for all rats. Immediately after lights out, the rats were moved to the testing cage where the two diets were presented side by side in two glass jars for three hours. Jar position was randomly switched during the trial and test days to prevent a place preference. The familiarization trials were necessary to expose the rats to both diets so that food preference tests would not be affected by novelty (Rolls & Rolls, 1973). In addition, two to three exposures of a similar high fat diet have been shown to reduce novelty in most rats on a chow diet (Baker, Osman, & Bodnar, 2001). Rats were not food deprived prior to these trials. At 180 minutes, intake was measured and rats were moved back to their housing cages.

A baseline food preference test occurred the day following the third familiarization trial. Two hours prior to lights out, the rats were weighed and moved to their testing cage, which did not have any food. At lights out, rats were presented with both high fat and low fat diet under red light illumination and intake was assessed at 30, 60, 120, and 180 minutes. Intake was measured to the nearest 0.1g and accounted for

spillage. Rats were then moved back the housing cage and resumed their previously allocated diet.

The food preference drug tests with quinpirole administration commenced the day after baseline testing. Two hours prior to lights out, the rats were weighed and moved to their testing cage, which did not have any food. Quinpirole was administered 30 minutes prior to lights out.

Results

Statistical Analyses

Dependent variables that were analyzed include the following: body weight, energy intake and fat preference. Energy intake is defined as the total calories of high and low fat diet consumed divided by the rat's weight in kilograms. Fat preference is defined as total amount of high fat food calories consumed divided by energy intake. All statistical analyses for each dependent variable are listed in Table 2. For clarification, test time #1 encompasses all the testing done during weeks 8-10 which includes the 24 hour intake test, baseline #1, and drug test #1, and test time #2 which occurred during weeks 16-18 and includes the 24 hour intake test, baseline #2, and drug test #2 (see Table1).

Body Weight

A two way (2 X 3) mixed ANOVA was conducted to look for weight differences between the HF and LF groups at three different time periods: baseline #1, #2, and at the end of the experiment. An alpha level of .05 was used for all statistical tests. The HF group (M = 444.3, SD = 9.7) and the LF group (M = 441.0, SD = 10.1) were similar in weight and there was not a significant main effect for diet group, F (1, 23) = .04, p = .845, η^2 = .00. There was a significant main effect for time period, F (2, 46) = 302.41, p < .001, η^2 = .93, and this was followed by dependent measures t-tests. The combined weight of the HF and LF groups at baseline #1 (M = 411.1, SD = 33.3) was significantly lower than at baseline #2 (M = 454.5, SD = 34.8) and at the end of the test (M = 463.3,

SD = 36.8), *t*(24) = -17.79, *p* < .001, *d* = 1.27, and *t*(24) = -16.92, *p* < .001, *d* = 1.49, respectively. The combined weight at baseline #2 was also significantly lower compared to at the end of the experiment, *t*(24) = -4.64, *p* < .001, *d* = .25.

There was a significant interaction between diet group and time period, *F* (2, 46) = 6.19, *p* = .004, η^2 = .21, (refer to Figure 2). This was followed by repeated measures ANOVA on the separate diet groups across all three time periods. The LF group had a significant difference in weight, *F* (2, 22) = 307.25, *p* < .001, η^2 = .97, and this was followed by dependent measures t-tests. The LF group weighed significantly less at baseline #1 (*M* = 405.2, *SD* = 29.3) compared to baseline #2 (*M* = 453.8, *SD* = 37.1), and end of the experiment (*M* = 465.6, *SD* = 39.2), *t*(11) = -18.09, *p* < .001, *d* = 1.45, and *t*(11) = -18.51, *p* < .001, *d* = 1.75, respectively. The weight of the LF group was also significantly lower at baseline #2 compared to the end of the experiment, *t*(11) = -8.04, *p* < .001, *d* = .31. The HF group also had a significant difference in weight over the three time periods, *F* (2, 24) = 86.25, *p* < .001, η^2 = .88. The HF group weighed significantly less at baseline #1 (*M* = 416.6, *SD* = 37.0) compared to baseline #2 (*M* = 455.2, *SD* = 34.2), *t*(12) = -10.81, *p* < .001, *d* = 1.08, and to the end of the experiment (*M* = 461.2, *SD* = 35.8), *t*(12) = -10.66, *p* < .001, *d* = 1.22. Unlike the LF group, the weight of the HF group did not significantly change from baseline #2 to end of the experiment, *t*(12) = -1.84, *p* = .091. Overall, both the HF and LF groups significantly gained weight over the time periods and were not significantly different from each other. However, the HF group only gained a significant amount of weight through baseline #2, while the LF group gained a significant amount of weight throughout the experiment.

Test Time 1.

Energy Intake.

Baseline #1.

To investigate the differences in energy intake (total calories/kg body weight) between the HF and LF groups at baseline #1, separate two-tailed independent samples t-tests were conducted at all time periods. Refer to Table 3 (interval intake) and 4 (cumulative intake) for all means and standard deviations and Table 5 for all *t*, *p* and *d* values. The LF group had significantly higher energy intake at all time periods (*p* ranges from .000-.021) compared to the HF group, except at the 60-120 minute interval (*p* = .162).

Drug Test #1.

A two-tailed dependent measures t-test was used to compare energy intake at baseline #1 and vehicle at all time periods, to determine if baseline measurements should be included in the drug dose comparison. Refer to Table 6 for all *t*, *p* and *d* values, and refer to Tables 3 and 4 for all means and standard deviations. The only significant difference occurred at the 0-30 minute interval, where the combined HF and LF groups had significantly higher energy intake with the vehicle ($M = 54.1$, $SD = 30.1$) compared to baseline intake ($M = 40.4$, $SD = 12.4$), $t(24) = 2.49$, $p = .020$, $d = .60$. Therefore, the 0-30 minute time interval was analyzed with a two way (2 X 5) mixed ANOVA with diet group (HF and LF group) as the between factor and drug dose (baseline, vehicle, low, medium, and high dose) as the within factor. All other time periods were analyzed with a two way (2 X 4) mixed ANOVA with only vehicle (0), low (.01), medium (.05), and high

(.1) dose as the within factor. In the few cases the assumptions of normality and homogeneity of covariance were violated in the ANOVA, Greenhouse-Geisser adjusted F values and df are reported. All significant main effects of drug dose were followed by two-tailed dependent measures t-tests to investigate differences between the doses. All significant interactions were followed by repeated measures ANOVAs for each diet group across all drug doses. A significant result was followed by two-tailed dependent measures t-tests to look for differences between the doses.

Interval Intake.

During the 0-30 minute interval, there was a significant main effect on energy intake for diet group, in which the HF group (M = 30.5, SD = 6.1) had a lower energy intake compared to the LF group (M = 51.0, SD = 7.5), F (1, 23) = 29.79, p < .001, η^2 =.56. The drug dose had a significant main effect on energy intake, F (2.4, 54.4) = 8.97, p < .001, η^2 =.28, and all means and standard deviations are in Table 3. Dependent t-tests showed the amount of energy intake was significantly decreased in the high dose compared to the low dose, t(24) = 2.94, p = .007, d = .64, vehicle, t(24) = 4.57, p = .000, d = .99, and baseline, t(24) = 3.75, p = .001, d = .71, but not the medium dose, t(24) = 1.53, p = .139. Energy intake was significantly decreased in the medium dose compared to the low dose, t(24) = 2.20, p = .037, d = .37, and vehicle, t(24) = 3.39, p = .002, d = .79, but not the baseline, t(24) = 1.76, p = .092. The low dose significantly suppressed energy intake compared to the vehicle, t(24) = 2.13, p = .042, d = .50, but not baseline, t(24) = -.29, p = .778. Energy intake was also significantly lower during baseline compared to vehicle, t(24) = -2.49, p = .020, d = .60. There was not a significant

interaction for diet group and drug dose, $F(2.4, 54.4) = 1.51$, $p = .207$, $\eta^2 = .06$. Generally, energy intake decreased as the dose of quinpirole increased during the 0-30 minute interval.

There was a significant main effect for diet group on energy intake during the 30-60 minute interval, and the HF group ($M = 7.0$, $SD = 6.4$) consumed significantly less than the LF group ($M = 20.0$, $SD = 14.6$), $F(1, 23) = 22.53$, $p < .001$, $\eta^2 = .50$. There was a significant main effect for drug dose, $F(3, 69) = 4.14$, $p = .009$, $\eta^2 = .15$, and all means and standard deviations are shown in Table 3. Energy intake was significantly lower at the high dose compared to the vehicle and low dose, $t(24) = 2.52$, $p = .019$, $d = .55$ and $t(24) = 3.26$, $p = .003$, $d = .66$, respectively. Energy intake was not significantly different for any of the other doses and all t, p, and d values are shown in Table 7. There was a significant interaction between diet group and the drug dose, $F(3, 69) = 3.89$, $p = .013$, $\eta^2 = .15$. The repeated measures ANOVA showed significant differences in the energy intake of the LF group, $F(3, 33) = 4.12$, $p = .014$, $\eta^2 = .27$. Energy intake at the medium and high dose was significantly lower than the low dose, $t(11) = 2.84$, $p = .016$, $d = 1.10$ and $t(11) = 3.79$, $p = .003$, $d = 1.22$, respectively. There were not any other significant differences and all other t, p, and d values can be seen in Table 7. The HF group did not have any significant differences in energy intake across the four drug doses, $F(3, 36) = 1.34$, $p = .276$, $\eta^2 = .10$. The increased doses of quinpirole significantly decreased energy intake for the LF group, and did not affect the energy intake in the HF group during the 30-60 minute interval.

During the 60-120 minute interval, the HF group (M = 12.5, SD = 2.1) had significantly higher energy intake than the LF group (M = 29.7, SD = 7.0), as shown by the main effect, F (1, 23) = 31.01, p < .001, η^2 =.57. There was a significant main effect for drug dose, F (2.3, 53.8) = 9.53, p < .001, η^2 =.29, and all means and standard deviations are in Table 3. Energy intake at the high dose was significantly less than the low dose and vehicle, t(24) = 3.97, p = .001, d = .92 and t(24) = 3.89, p = .001, d = 1.07, respectively. The medium dose significantly decreased energy intake compared to the low dose, t(24) = 2.18, p = .040, d = .53, and vehicle, t(24) = 3.10, p = .005, d = .75. Energy intake was not different between the vehicle and low dose, and between the medium and high dose (all t, p, and d values are in Table 8). There was a significant diet by dose interaction, F (2.3, 53.8) = 3.07, p = .047, η^2 =.12. The repeated measures ANOVA showed a significant main effect for the LF group, F (3, 33) = 6.25, p = .002, η^2 = .36. The high dose produced a significant decrease in energy intake compared to the vehicle dose and the low dose, t(11) = 3.86, p = .003, d = 1.65 and t(11) = 4.23, p = .001, d = 1.49, respectively. There was a main effect for the HF group, F (3, 36) = 4.32, p = .011, η^2 = .27. Energy intake was significantly lower at the medium dose compared to the vehicle, t(12) = 2.77, p = .017, d = 1.22. Energy intake was not significantly different at any other drug dose comparisons. During the 60-120 minute interval, the HF group had significantly less energy intake than the LF group and the medium and high dose effectively decreased energy intake.

There was a significant main effect for diet group during the 120-180 minute interval, and the HF group (M =17.3, SD = 10.7) had significantly lower energy intake

than the LF group (M=44.9, SD = 23.2), F (1, 23) = 45.44, p < .001, η^2 =.66. There was a significant main effect for drug dose, F (2.3, 53.2) = 3.52, p = .031, η^2 =.13, and all means and standard deviations can be seen in Table 3. Energy intake at the high dose was significantly less compared to the medium dose, t(11) = 3.42, p = .002, d = .70, low dose, t(24) = 2.58, p = .017, d = .62, and vehicle, t(11) = 2.38, p = .026, d = .48. Energy intake was not significantly different by the vehicle compared to the low and medium dose, t(11) = -.45, p = .661 and t(11) = -1.00, p = .329, respectively. There was no difference between the low and medium dose, t(11) = -.72, p = .480. The interaction between diet group and drug dose was not significant, F (2.3, 53.2) = .78, p = .480, η^2 =.03. Energy intake was significantly decreased by the high dose, while energy intake was stable across all other doses during the 120-180 minute interval.

Cumulative Intake.

The HF group (M = 35.2, SD = 7.7) had a significantly lower energy intake than the LF group (M = 68.9, SD = 10.1) during 0-60 minute time period, as shown by the main effect, F (1, 23) = 45.59, p < .001, η^2 = .67. There was also a main effect for drug dose, F (1.8, 41.6) = 13.13, p < .001, η^2 = .36, and all means and standard deviations are shown in Table 4. Energy intake with the high dose was significantly less than with the low dose, t(24) = 4.68, p < .001, d = .80, and the vehicle, t(24) = 4.83, p < .001, d = 1.00, but not the medium dose, t(24) = 1.84, p = .078. Energy intake at the medium dose was significantly lower than the low dose, t(24) = 3.04, p = .006, d = .52, and the vehicle, t(24) = 3.25, p = .003, d = .78. Energy intake was not significantly different between the vehicle and low dose, t(24) = 1.80, p = .085. The interaction between diet group and drug

dose was not significant, $F(1.8, 41.6) = 2.34$, $p = .113$, $\eta^2 = .09$. Overall, the HF group had a lower energy intake than the LF group, and energy intake decreased as the dose of quinpirole increased for both groups.

During the 0-120 minute time period, the HF group ($M = 47.7$, $SD = 15.5$) had significantly lower energy intake than the LF group ($M = 98.6$, $SD = 27.0$), $F(1, 23) = 55.10$, $p < .001$, $\eta^2 = .71$. There was also a significant main effect for drug dose, $F(1.6, 36.8) = 32.43$, $p < .001$, $\eta^2 = .59$. Refer to Table 9 for all t, p, and d values and to Table 4 for all means and standard deviations. Energy intake was significantly decreased at the high dose compared to the medium dose, low dose, and vehicle. The medium dose significantly decreased energy intake compared to the low dose and vehicle, and the low dose significantly decreased energy intake compared to the vehicle. There was a significant interaction between the diet group and the drug dose, $F(1.6, 36.8) = 6.51$, $p = .006$, $\eta^2 = .22$. There were significant differences among the drug doses for the LF group, $F(1.5, 16.3) = 20.65$, $p < .001$, $\eta^2 = .65$. Energy intake was significantly lower at the high dose compared to the medium dose, low dose, and vehicle. The medium dose significantly lowered energy intake compared to the low dose and vehicle, but there was not a difference between the low dose and vehicle. There was also a main effect for the HF group, $F(3, 36) = 11.28$, $p < .001$, $\eta^2 = .49$. Energy intake at the high dose was significantly lower than the low dose and vehicle, but not the medium dose. Energy intake was significantly decreased by the medium dose compared to the low dose and vehicle, but there was again, no difference between the low dose and vehicle. Overall, the

HF group consumed less energy than the LF group, and both groups consumed significantly less energy as the dose of quinpirole increased.

The HF group ($M = 65.0$, $SD = 18.2$) had a significantly lower energy intake during the 0-180 minute time period than the LF group ($M = 143.6$, $SD = 38.5$), $F(1, 23) = 76.22$, $p < .001$, $\eta^2 = .77$. There was also a main effect for drug dose, $F(2.5, 51.7) = 24.61$, $p < .001$, $\eta^2 = .52$. All means and standard deviations are in Table 4 and all t, p, and d values are in Table 10. Energy intake at the high dose was significantly lower than the medium dose, low dose, and vehicle. The medium dose significantly lowered energy intake compared to the low dose and vehicle, but the difference in energy intake between the vehicle and low dose was not significant. There was a significant interaction between the diet group and drug dose, $F(2.5, 51.7) = 5.69$, $p = .004$, $\eta^2 = .20$, which is shown in Figure 2. A repeated measures ANOVA showed a significant main effect for the LF group, $F(3, 33) = 15.78$, $p < .001$, $\eta^2 = .59$, and the HF group, $F(3, 36) = 8.75$, $p < .001$, $\eta^2 = .42$. Dependent measures t-tests showed both the LF and HF groups had the same pattern of significant differences between drug doses. Energy intake was significantly lower with the high dose compared to the medium dose, low dose, and vehicle. The medium dose significantly decreased energy intake compared to the vehicle, but not the low dose. Energy intake with the low dose was not significantly different than with vehicle. Overall, the HF group had a significantly lower energy intake compared to the LF group, but both groups showed a similar pattern of decreased energy intake with an increased dose of quinpirole.

Fat Preference.

Baseline #1.

To determine if there were differences in fat preference between the HF and LF group at baseline #1, independent measures t-tests were used to analyze all time periods. All means and standard deviations are shown in Table 11 (interval intake) and 12 (cumulative intake), and all *t*, *p*, and *d* values are shown in Table 13. Neither the HF nor the LF group showed more preference for high fat food at baseline #1.

Drug Test #1.

Two-tailed dependent measures t-tests were used to compare fat preference scores for both groups between baseline #1 and vehicle at all time periods. All means and standard deviations are shown in Table 11 and 12, and all *t*, *p*, and *d* values are shown in Table 14. The only significant difference occurred during the 0-120 minute time period, in which high fat food was more preferred during baseline ($M = .38$, $SD = .04$) than vehicle ($M = .36$, $SD = .07$), $t(24) = 2.06$, $p = .050$, $d = .35$. Therefore, the 0-120 minute time period was analyzed by a two way (2 X 5) mixed ANOVA comparing diet group (HF and LF) as the between factor and drug dose (baseline, vehicle, low, medium, and high dose) as the within factor. All other time periods were analyzed with a two way (2 X 4) mixed ANOVA with only vehicle, low, medium and high dose as the within factor. All significant main effects of drug dose were followed up by two-tailed dependent t-tests to investigate differences between the doses. All significant interactions were followed up by repeated measures ANOVAs for each diet group across all drug doses. Significant results were followed by two-tailed dependent measures t-tests to look for differences between the doses.

Interval Intake.

During the 0-30 minute time period, there was a significant main effect for diet group with the HF group ($M = .22$, $SD = .11$) displaying less preference for high fat food than the LF group ($M = .28$, $SD = .08$), $F(1, 23) = 4.94$, $p = .036$, $\eta^2 = .18$. There was a significant main effect for drug dose, $F(3, 69) = 12.80$, $p < .001$, $\eta^2 = .36$. Means and standard deviations are shown in Table 11. Compared to the vehicle, fat preference was significantly less in the high dose, $t(24) = 5.41$, $p < .001$, $d = 1.34$, medium dose, $t(24) = 6.32$, $p < .001$, $d = 1.37$, and the low dose, $t(24) = 3.94$, $p = .001$, $d = .95$. There were no significant differences in fat preference between the low dose compared to the medium dose, $t(24) = 1.45$, $p = .161$, and the high dose, $t(24) = 1.90$, $p = .070$. Fat preference was also not significantly different between the medium dose and the high dose, $t(24) = .62$, $p = .544$. There was not a significant interaction between the diet groups and the drug doses, $F(3, 69) = 2.40$, $p = .075$, $\eta^2 = .10$. In the 0-30 minute time period, the HF group preferred fat less than the LF group, and fat preference for both groups decreased at all drug doses compared to the vehicle.

There was no main effect for diet group during the 30-60 minute time interval, $F(1, 23) = .35$, $p = .716$, $\eta^2 = .01$, in which fat preference was not different between the HF ($M = .23$, $SD = .20$) and LF groups ($M = .24$, $SD = .13$). There was a significant main effect for drug dose, $F(3, 69) = 5.16$, $p = .003$, $\eta^2 = .18$. Means and standard deviations are shown in Table 11. Fat preference was significantly decreased at the high dose compared to the low dose and vehicle, $t(24) = 2.77$, $p = .001$, $d = .83$ and $t(24) = 2.98$, $p = .007$, $d = .94$, respectively. There were no significant differences between the vehicle

compared to the low dose, $t(24) = .42$, $p = .679$, and the medium dose, $t(24) = 1.09$, $p = .285$. Fat preference was also not significantly different at the medium dose compared to the low dose, $t(24) = .87$, $p = .396$ and the high dose, $t(24) = 2.03$, $p = .054$.

There was a significant interaction in fat preference between the diet group and drug dose during the 30-60 minute time interval, $F(3, 69) = 4.56$, $p = .006$, $\eta^2 = .17$. The main effect was not significant for the HF group, $F(3, 36) = .17$, $p = .916$, $\eta^2 = .01$, but was significant for the LF group, $F(3, 33) = 14.59$, $p < .001$, $\eta^2 = .57$. Means and standard deviations are shown in Table 11. Fat preference in the LF group was significantly decreased at the high dose compared to the medium dose, $t(11) = 4.31$, $p = .001$, $d = 1.56$, low dose, $t(11) = 9.88$, $p < .001$, $d = 4.00$, and vehicle, $t(11) = 6.40$, $p < .001$, $d = 2.48$. Fat preference at vehicle was not significantly different from the low dose, $t(11) = -.44$, $p = .667$, or the medium dose, $t(11) = 1.29$, $p = .224$, and was also not significantly different between the low dose and the medium dose, $t(11) = 1.53$, $p = .154$. Overall, fat preference was significantly lower at the high dose, and results of the interaction showed that fat preference was significantly lower at the high dose in the LF group.

Fat preference in the HF ($M = .27$, $SD = .18$) and the LF group ($M = .29$, $SD = .13$) was not significantly different during the 60-120 minute interval, $F(1, 23) = .51$, $p = .483$, $\eta^2 = .02$. There was a significant main effect for drug dose, $F(3, 69) = 3.50$, $p = .020$, $\eta^2 = .13$, and means and standard deviations are shown in Table 11. Fat preference at the high dose was significantly lower than the low dose and vehicle, $t(24) = 3.13$, $p = .005$, $d = .85$ and $t(24) = 2.57$, $p = .017$, $d = .70$, respectively. Fat preference at the

medium dose was not significantly different than vehicle $t(24) = .65$, $p = .519$, low dose, $t(24) = 1.09$, $p = .289$, and high dose, $t(24) = 1.37$, $p = .183$. Fat preference was also not significantly different between vehicle and the low dose, $t(24) = -.60$, $p = .554$. The interaction between diet group and drug dose was also not significant, $F(3, 69) = 2.65$, $p = .056$, $\eta^2 = .10$. Fat preference was not different between diet groups, and both groups combined showed significantly less fat preference with the high dose.

Fat preference during the 120-180 minute did not show a main effect for diet group, $F(1, 23) = 3.66$, $p = .068$, $\eta^2 = .14$, in which there was not a difference in fat preference between the HF ($M = .29$, $SD = .14$) and LF groups ($M = .34$, $SD = .10$). There was not a main effect for drug dose, $F(3, 69) = 1.33$, $p = .272$, $\eta^2 = .06$, and there was not an interaction between diet group and drug dose, $F(3, 69) = 1.40$, $p = .250$, $\eta^2 = .06$. Means and standard deviations are shown in Table 11. Diet group and drug dose did not significantly affect fat preference during the 120-180 minute interval.

Cumulative Interval.

During the 0-60 minute time period, the HF group ($M = .23$, $SD = .08$) significantly preferred high fat food less than the LF group ($M = .28$, $SD = .07$), $F(1, 23) = 4.59$, $p = .043$, $\eta^2 = .17$. There was a significant main effect for drug dose, $F(3, 69) = 27.81$, $p < .001$, $\eta^2 = .55$. Means and standard deviations are shown in Table 12 and all t, p, and d values are in Table 15. Fat preference was significantly less at the high dose compared to the medium dose, low dose, and vehicle. The medium dose significantly decreased fat preference compared to the low dose and vehicle, and the low dose significantly decreased fat preference compared to vehicle. There was not a significant

interaction between the diet group and the drug dose, $F(3, 69) = 1.02$, $p = .389$, $\eta^2 = .04$. The LF group preferred the high fat food more than the HF group, and both groups together had a significant dose dependent decrease in fat preference.

The HF group ($M = .28$, $SD = .07$) had a similar preference for high fat food as the LF group ($M = .31$, $SD = .05$) during the 0-120 minute time period, and the main effect was not significant, $F(1, 23) = 4.59$, $p = .043$, $\eta^2 = .13$. There was a significant main effect for drug dose, $F(4, 92) = 44.41$, $p < .001$, $\eta^2 = .66$. Means and standard deviations are shown in Table 12 and all follow up t, p, and d values are shown in Table 15. Fat preference was significantly decreased at the high dose compared to the medium dose, low dose, vehicle, and baseline. Fat preference at the medium dose was significantly lower than at the low dose, vehicle, and baseline. Fat preference was also significantly lower at the low dose compared to the vehicle and baseline, and vehicle was significantly lower than baseline. The interaction between diet group and drug dose was not significant, $F(4, 92) = .69$, $p = .603$, $\eta^2 = .03$. All doses of quinpirole and vehicle significantly decreased fat preference in both diet groups in a dose dependent manner.

There was a significant main effect for diet group during the 0-180 minute time period, with the HF group ($M = .28$, $SD = .07$) showing less fat preference than the LF group ($M = .37$, $SD = .04$), $F(1, 23) = 31.68$, $p < .001$, $\eta^2 = .58$. The drug dose did show a significant main effect, $F(3, 69) = 16.62$, $p < .001$, $\eta^2 = .42$, with means and standard deviations shown in Table 12 and all follow up t, p, and d values are shown in Table 15. Fat preference was significantly decreased by the high dose compared to the medium dose, low dose, and vehicle. Fat preference at the medium dose was significantly lower

than vehicle, but not the low dose. There was no difference in fat preference between the vehicle and low dose. There was not a significant interaction between diet group and drug dose, $F(3, 69) = 2.65$, $p = .055$, $\eta^2 = .10$, and results are displayed in Figure 3. Over 180 minutes at test time #1, the HF group showed significantly less preference for high fat food than the LF group, and fat preference significantly decreased in a dose dependent manner.

Test Time 2

Energy Intake.

Baseline #2.

Separate two-tailed independent samples t- tests were conducted at every time period to investigate energy intake differences between the HF and LF groups at baseline #2. All means and standard deviations are shown in Table 16 (interval intake) and Table 17 (cumulative intake), and all *t*, *p*, and *d* values are shown in Table 18. Energy intake was not significantly different between the HF and LF groups at any of the time periods. These results are notably different from baseline #1, where the LF group had significantly higher energy intake than the HF group at every time period.

Drug Test #2.

To determine if there were differences in energy intake at baseline #2 compared to vehicle for both diet groups combined, dependent measures t-tests were conducted at all time periods. All means and standard deviations are shown in Table 16 and Table 17, and all *t*, *p*, and *d* values are shown in Table 19. There were no significant differences in

energy intake, and therefore, only vehicle was used for all drug dose comparisons at all time periods. Energy intake was analyzed with a two way (2 X 4) mixed ANOVA at all time periods to compare the HF and LF groups (between factor) across the vehicle, low, medium, and high dose (within factor). All significant main effects of drug dose were followed up by two-tailed dependent measures t-tests to investigate differences between the doses. All significant interactions were followed up by repeated measures ANOVAs for each diet group across all drug doses. A significant result was followed by two-tailed dependent measures t-tests to look for differences between the doses.

Interval Intake.

During the 0-30 minute time period, there was a main effect for diet group and the HF group, (M = 42.8, SD = 14.6) had significantly lower energy intake than the LF group (M = 50.9, SD = 17.8), F (1, 23) = 4.40, p = .047, η^2 = .16. There was a main effect for drug dose, F (3, 69) = 19.25, p < .001, η^2 = .46, and all means and standard deviations are shown in Table 16. Energy intake was significantly lower with the high dose compared to the low dose, t(24) = 5.19, p < .001, d = 1.26, and vehicle, t(24) = 5.12, p < .001, d = 1.46, but not the medium dose, t(24) = 1.22, p = .234. Energy intake at the medium dose was significantly lower compared to the low dose, t(24) = 4.40, p < .001, d = 1.07, and vehicle, t(24) = 4.69, p < .001, d = 1.31. There were no differences between vehicle and the low dose, t(24) = 1.87, p = .074. The interaction between diet group and drug dose was not significant, F (3, 69) = 2.52, p = .065, η^2 = .10. The HF group had significantly lower energy intake than the LF group, and both groups had significantly less energy intake with the high and medium doses of quinpirole in the first 30 minutes.

A significant main effect was found for diet group during the 30-60 minute time interval, and the HF group, (M = 14.0, SD = 11.6) had lower energy intake than the LF group (M = 20.7, SD = 13.4), F (1, 23) = 5.48, p = .028, η^2 = .19. The main effect for drug dose was significant, F (3, 69) = 11.40, p < .001, η^2 = .33, and all means and standard deviations are in Table 16. Energy intake was significantly lower at the high dose compared to the medium dose, t(24) = 3.07, p = .005, d = .88, low dose, t(24) = 3.61, p = .001, d = .94, and vehicle, t(24) = 6.15, p < .001, d = 1.78. The medium dose significantly decreased energy intake compared to vehicle, t(24) = 3.12, p = .005, d = .73, but not the low dose, t(24) = .10, p = .921. Energy intake was also significantly lower at the low dose compared to vehicle, t(24) = 2.47, p = .021, d = .72. There was not a significant interaction between the diet group and drug dose, F (3, 69) = .56, p = .642, η^2 = .02. The HF group continued to have a decreased amount of energy intake compared to the LF group, and all doses of quinpirole were effective at decreasing energy intake compared to vehicle.

During the 60-120 minute interval, energy intake between the HF (M = 14.7, SD = 13.4) and LF group (M = 14.9, SD = 12.5) was not significantly different, F (1, 23) = .01, p = .934, η^2 = .00. There was not a significant main effect for drug dose, F (3, 69) = .52, p = .671, η^2 = .02, and the interaction between diet group and drug dose was also not significant, F (3, 69) = .98, p = .410, η^2 = .04. Means and standard deviations are shown in Table 16. Neither diet group, nor drug dose had a significant effect on energy intake during the 60-120 minute interval.

There was not a main effect for diet group during the 120-180 minute interval, and the HF (M = 30.0, SD = 14.3) and LF group (M = 31.0, SD = 16.6) did not have a significant difference in energy intake, F (1, 23) = .43, p = .520, η^2 = .02. Drug dose had a significant main effect, F (3, 69) = 7.01, p < .001, η^2 = .23, and means and standard deviations are shown in Table 16. Interestingly, energy intake with the vehicle was significantly lower than the medium dose, t(24) = -2.13, p = .044, d = .45. Energy intake with the high dose was also significantly lower than the medium dose and the low dose, t(24) = 3.71, p = .001, d = .86. There were no differences in energy intake between vehicle, t(24) = 4.50, p < .001, d = .96, and the low dose, t(24) = -1.54, p = .136, and the high dose, t(24) = 2.03, p = .054, and between the low dose and the medium dose, t(24) = -.55, p = .591. The interaction between diet group and drug dose was also not significant, F (3, 69) = 1.94, p = .131, η^2 = .08. During the 120-180 minute interval, energy intake was not different between the diet groups, however energy intake was highest with the medium dose and lowest with the high dose.

Cumulative Intake.

There was a significant main effect for diet group during the 0-60 minute time period, in which the HF group (M = 56.8, SD = 15.6) had a lower intake of energy than the LF group (M = 71.5, SD = 15.6), F (1, 23) = 9.42, p = .005, η^2 = .29. Drug dose produced a significant main effect, F (3, 69) = 42.00, p < .001, η^2 = .65, and means and standard deviations are shown in Table 17. Energy intake was significantly lower at the high dose compared to the medium dose, t(24) = 3.50, p = .002, d = .87, low dose, t(24) = 8.28, p < .001, d = 1.57, and vehicle, t(24) = 9.72, p < .001, d = 2.45. The medium dose

significantly decreased energy intake compared to the low dose, $t(24) = 43.12$, $p = .005$, $d = .80$, and vehicle, $t(24) = 6.40$, $p < .001$, $d = 1.71$. Energy intake was also significantly decreased at the low dose compared to vehicle, $t(24) = 4.44$, $p < .001$, $d = .88$. The interaction between diet group and drug dose was not significant, $F(3, 69) = 1.00$, $p = .400$, $\eta^2 = .04$. Energy intake was significantly lower in the HF group compared to the LF group, and it significantly decreased in a dose dependent manner.

During the 0-120 minute time period, there was a main effect for diet group and the HF group ($M = 71.5$, $SD = 20.2$) had significantly lower energy intake compared to the LF group ($M = 86.4$, $SD = 25.4$), $F(1, 23) = 5.64$, $p = .026$, $\eta^2 = .20$. There was a significant main effect for drug dose, $F(3, 69) = 32.19$, $p < .001$, $\eta^2 = .58$, and means and standard deviations are shown in Table 17. Energy intake with the high dose was significantly less than the medium dose, $t(24) = 2.80$, $p = .010$, $d = .69$, low dose, $t(24) = 5.51$, $p < .001$, $d = 1.15$, and vehicle, $t(24) = 8.35$, $p < .001$, $d = 2.17$. Energy intake with the medium dose was significantly lower than with the low dose, $t(24) = 2.52$, $p = .019$, $d = .59$, and vehicle, $t(24) = 5.88$, $p < .001$, $d = 1.58$, and the low dose was significantly lower than the vehicle, $t(24) = 4.29$, $p < .001$, $d = .85$. The diet group and drug dose interaction was not significant, $F(3, 69) = 1.88$, $p = .141$, $\eta^2 = .08$. Similar to the 0-60 time period, energy intake in the 0-120 minute time period was lower in the HF group, and significantly decreased as the dose of quinpirole increased.

There was not a significant difference in energy intake between the HF group ($M = 99.4$, $SD = 25.5$) and the LF group ($M = 117.4$, $SD = 29.8$) during the 0-180 minute time period, $F(1, 23) = 3.78$, $p = .064$, $\eta^2 = .14$. There was a significant main effect for

drug dose, $F(3, 69) = 43.92$, $p < .001$, $\eta^2 = .66$. All means and standard deviations are shown in Table 17 and all *t*, *p*, and *d* values are shown in Table 20. Energy intake was significantly lower with the high dose compared to the medium dose, low dose, and vehicle. The medium dose significantly decreased energy intake compared to the low dose and vehicle, and the low dose significantly decreased energy intake compared to the vehicle. There was also a significant interaction between diet group and drug dose, $F(3, 69) = 4.31$, $p = .008$, $\eta^2 = .16$, which was followed up by a repeated measures ANOVA on each diet group. Results are shown in Figure 4. There was a main effect for drug dose in the HF group, $F(3, 69) = 14.04$, $p < .001$, $\eta^2 = .54$. Energy intake with the high dose was significantly lower than with the medium dose, low dose, and vehicle. Energy intake with the low and medium dose was significantly lower than the vehicle, but there was no difference between the low and medium dose. There was a significant difference in energy intake across all doses for the LF group, $F(3, 33) = 30.37$, $p < .001$, $\eta^2 = .74$. Energy intake was significantly lower with the high dose compared to the medium dose, low dose, and vehicle. Energy intake with the medium dose was significantly lower than the low dose and vehicle, but there was not a difference between the low dose and vehicle. Overall, quinpirole significantly decreased energy intake in both diet groups in a dose dependent manner.

Fat Preference.

Baseline #2.

To determine differences in fat preference between the HF and LF group at baseline #2, separate two-tailed independent samples t-tests were conducted at all time periods. All means and standard deviations are shown in Table 21 (interval intake) and 22 (cumulative intake), and all *t*, *p*, and *d* values are shown in Table 23. The HF group had significantly less fat preference compared to the LF group during 30-60 minutes and 60-120 minutes, $t(13) = 2.59$, $p = .023$, $d = 1.04$, and $t(15) = 3.31$, $p = .005$, $d = 1.28$, respectively. This is contrary to baseline #1, where fat preference was not different between the groups at any time period.

Drug Test #2.

Two-tailed dependent measures t-tests were used to analyze differences between baseline #2 and vehicle at all time periods, to determine if baseline should be included in the drug dose analysis. All means and standard deviations are shown in Table 21 and 22, and all *t*, *p*, and *d* values are shown in Table 24. Both diet groups combined had significantly higher fat preference at baseline compared to vehicle during the 0-30 and 0-180 minute time periods, $t(24) = 2.44$, $p = .022$, $d = .42$, and $t(24) = 2.10$, $p = .046$, $d = .30$, respectively. Therefore, those time periods were analyzed with a two way (2 X 5) mixed ANOVA, with HF and LF as the between factor, and baseline, vehicle, low, medium, and high as the within factor. All other time periods were analyzed with a two way (2 X 4) mixed ANOVA, with HF and LF as the between factor and vehicle, low, medium, and high as the within factor. In the few cases the assumptions of normality and homogeneity of covariance were violated in the ANOVA, Greenhouse-Geisser adjusted *F*

values and *df* are reported. All significant main effects of drug dose were followed up by two-tailed dependent measures t-tests to investigate differences between the doses.

Interval Intake.

Fat preference was not significantly different between the HF ($M = .33$, $SD = .10$) and LF group ($M = .31$, $SD = .07$) during the 0-30 minute time period, $F(1, 23) = .50$, $p = .488$, $\eta^2 = .02$. There was a significant main effect for drug dose, $F(2.9, 65.8) = 46.89$, $p < .001$, $\eta^2 = .67$. All means and standard deviations are shown in Table 21, and all *t*, *p*, and *d* values are shown in Table 25. Fat preference was significantly lower at the high dose compared to the low dose, vehicle, and baseline, but not the medium dose. Fat preference at the medium dose was significantly lower than at the low dose, vehicle, and baseline. The low dose significantly decreased fat preference compared to vehicle and baseline. Fat preference was also significantly lower at the vehicle compared to baseline. The interaction between diet group and drug dose was not significant, $F(2.9, 65.8) = .53$, $p = .657$, $\eta^2 = .02$. All injections significantly decreased fat preference in both diet groups in a dose-dependent manner.

During the 30-60 minute interval, there were no differences in fat preference between the HF ($M = .26$, $SD = .18$) and LF group ($M = .34$, $SD = .16$), $F(1, 23) = 3.69$, $p = .067$, $\eta^2 = .14$. There was a significant main effect for drug dose, $F(3, 69) = 12.95$, $p < .001$, $\eta^2 = .36$, and means and standard deviations are shown in Table 21. Fat preference was significantly lower at the high dose compared to the medium dose, $t(24) = 3.01$, $p = .006$, $d = .89$, low dose, $t(24) = 3.53$, $p = .002$, $d = .92$, and vehicle, $t(24) = 7.38$, $p < .001$, $d = 2.06$. Fat preference was significantly lower at the medium dose compared

to vehicle, $t(24) = 2.794$, $p = .010$, $d = .822$, but not the low dose, $t(24) = .36$, $p = .72$. The low dose significantly lowered fat preference compared to vehicle, $t(24) = 2.44$, $p = .024$, $d = .67$. Diet group and drug dose did not have a significant interaction, $F(3, 69) = .93$, $p = .429$, $\eta^2 = .04$. Both diet groups significantly decreased fat preference as the dose of quinpirole increased.

There was no main effect for diet group during the 60-120 minute interval, in which the HF group ($M = .25$, $SD = .22$) did not differ in fat preference from the LF group ($M = .27$, $SD = .20$), $F(1, 23) = .11$, $p = .747$, $\eta^2 = .01$. There also was not a main effect for drug dose, $F(3, 69) = .60$, $p = .620$, $\eta^2 = .03$, or an interaction between diet group and drug dose, $F(3, 69) = .34$, $p = .797$, $\eta^2 = .02$. Means and standard deviations are shown in Table 21. Both diet group and drug dose did not have an effect on fat preference, and these results are similar to the energy intake results for this time interval.

Fat preference for the HF group ($M = .33$, $SD = .15$) did not significantly differ significantly from the LF group during the 120-180 minute interval ($M = .35$, $SD = .13$), $F(1, 23) = .35$, $p = .559$, $\eta^2 = .02$. There was a main effect for drug dose, $F(3, 69) = 4.18$, $p = .009$, $\eta^2 = .15$, and means and standard deviations are shown in Table 21. Fat preference was significantly lower at the high dose compared to the medium dose, $t(24) = 3.18$, $p = .004$, $d = .64$, low dose, $t(24) = 2.88$, $p = .008$, $d = .78$, and vehicle, $t(24) = 2.52$, $p = .019$, $d = .66$. There were no significant differences between vehicle and the low dose, $t(24) = -.30$, $p = .767$, and the medium dose, $t(24) = .08$, $p = .935$, and between the low and medium dose, $t(24) = .50$, $p = .624$. The interaction between diet group and drug dose was not significant, $F(3, 69) = 1.51$, $p = .221$, $\eta^2 = .06$. Fat preference for both

groups was significantly decreased at only the high dose during the 120-180 minute interval.

Cumulative Intake.

Fat preference was not significantly different in the HF group (M = .32, SD = .08) compared to the LF group (M = .31, SD = .07) during the 0-60 minute period, F (1, 23) = .44, p = .513, η^2 = .02. There was a significant main effect for drug dose, F (3, 69) = 41.67, p < .001, η^2 = .64. All means and standard deviations are shown in Table 22 and all t, p, and d values are shown in Table 26. Fat preference was significantly lower at the high dose compared to the medium dose, low dose, and vehicle. Fat preference at the medium dose was significantly lower than the low dose and vehicle, and the low dose was significantly lower than the vehicle. There was not a significant interaction between diet group and drug dose, F (3, 69) = .99, p = .405, η^2 = .04. There was a significant dose dependent decrease in fat preference during the 0-60 time period, with no effect from diet group.

During the 0-120 minute time period, fat preference in the HF group (M = .33, SD = .09) was not significantly different from the LF group (M = .32, SD = .07), F (1, 23) = .59, p = .452, η^2 = .03. Drug dose did have a significant main effect, F (3, 69) = 28.01, p < .001, η^2 = .55. All means and standard deviations are shown in Table 22 and all d, p, and t values are shown in Table 26. Similar to the 0-60 minute time period, fat preference was significantly lowered by the high dose compared to the medium dose, low dose, and vehicle. Fat preference was also significantly lowered by the medium dose compared to the low dose and vehicle, and also significantly lowered by the low dose compared to

vehicle. Diet group and drug dose did not have a significant interaction, $F(3, 69) = .29$, $p = .830$, $\eta^2 = .01$. The 0-120 minute time period also had a significant dose dependent decrease in fat preference.

For the 0-180 minute time period, there was not a main effect for diet group and the HF group ($M = .36$, $SD = .07$) did not differ from the LF group ($M = .36$, $SD = .05$), $F(1, 23) = .20$, $p = .661$, $\eta^2 = .01$. There was a main effect for drug dose, $F(2.6, 60.7) = 39.02$, $p < .001$, $\eta^2 = .63$. All means and standard deviations are shown in Table 22 and all d, p, and t values are shown in Table 26. Fat preference was significantly lower at the high dose compared to the medium dose, low dose, vehicle, and baseline. The medium dose significantly decreased fat preference compared to vehicle and baseline, but not the low dose. Fat preference at the low dose was significantly lower than at vehicle and baseline, and fat preference at vehicle was significantly lower than baseline. The interaction between diet group and drug dose was also not significant, $F(2.6, 60.7) = .48$, $p = .673$, $\eta^2 = .02$, and refer to Figure 5. Overall, diet group did not have a significant effect on fat preference, but all doses (including vehicle) had a significant dose dependent effect on fat preference during the 0-180 minute time period.

Test Time #1 versus Test Time #2

Fat Preference.

Separate two way (2 X 2) mixed ANOVAs were used to examine the differences in fat preference from test time #1 to test time #2 (within factor) and the HF and LF groups (between factor). An analysis was run at all four cumulative time periods (0-30, 0-

60, 0-120, and 0-180) for all four drug doses (vehicle, low, medium, and high). The results showed similarity among all the time periods for each drug dose; therefore, only one representative time period for each drug dose is discussed. All of the results are shown in Table 27 and 28, and all means and standard deviations are shown in Table 12 and 22. Refer to Figure 6 for overview of HF and LF group means at both test times across all drug doses.

During the 0-180 minute time period with the vehicle, there was not a significant difference in fat preference between the HF (M = .38, SD = .07) and LF group (M = .39, SD = .05), F (1, 23) = .41, p = .528, η^2 = .02. There was a significant main effect for test time that showed fat preference at test time #1 (M = .35, SD = .06) was significantly lower than at test time #2 (M = .42, SD = .04), F (1, 23) = 32.73, p < .001, η^2 = .59. The interaction between diet group and test time was not significant, F (1, 23) = .64, p = .433, η^2 = .03. All cumulative time periods at vehicle showed this result pattern, where there were no differences between the diet groups or interactions between the diet groups and test time. However, fat preference for both groups combined significantly increased from test time #1 to test time #2.

Fat preference with the low dose during the 0-180 minute time period was not significantly different between the HF (M = .33, SD = .08) and LF group (M = .35, SD = .04), F (1, 23) = 1.48, p = .237, η^2 = .06. Fat preference at test time #1 (M = .31, SD = .05) was significantly lower than at test time #2 (M = .36, SD = .07), F (1, 23) = 8.43, p = .008, η^2 = .27. Diet group and test time did not have a significant interaction, F (1, 23) = 1.74, p = .201, η^2 = .07. Similar results are seen at all other cumulative time periods with

the low dose of quinpirole. Diet group alone and interacting with test time did not have an effect on fat preference, but there was a significant increase from test time #1 to test time #2.

During the 0-180 minute time period, the HF (M = .31, SD = .07) and the LF group (M = .32, SD = .06) did not differ significantly from each other in fat preference at the medium dose, F (1, 23) = .06, p = .807, η^2 = .00. Test time #1 (M = .29, SD = .07) was significantly lower than test time #2 (M = .33, SD = .06) in fat preference, F (1, 23) = 9.73, p = .005, η^2 = .30. There was a significant interaction between diet group and test time, F (1, 23) = 6.99, p = .015, η^2 = .23, which was followed up by a two-tailed dependent measures t-test for each diet group. The HF group significantly increased fat preference from test time #1 (M = .27, SD = .08) to test time #2 (M = .35, SD = .06), t(12) = -3.32, p = .006, d = 1.13. The LF group did not change fat preference from test time #1 (M = .31, SD = .05) to test time #2 (M = .32, SD = .07), t(11) = -.54, p = .603. Although the HF and LF group were not significantly different from each other, they had a different pattern for fat preference from test time #1 to test time #2 with the medium dose. Both groups together had a significant increase in fat preference from test time #1 to test time #2, but separately only the HF group had a significant increase in fat preference. These results are similar to the 0-120 minute time period; however, the 0-60 minute time period did not have a significant interaction. The 0-30 minute time period did not show any significant difference in fat preference between the diet groups, test time, or an interaction of the two.

The only significant difference in fat preference by the high dose occurred during the 0-30 minute time period. The HF (M = .17, SD = .12) and LF (M = .22, SD = .12) group did not differ significantly from each other in fat preference, F (1, 23) = 2.17, p = .154, η^2 = .09. Also there was not a significant difference in fat preference between test time #1 (M = .19, SD = .13) and test time #2 (M = .19, SD = .12), F (1, 23) = .00, p = .963, η^2 = .00. The interaction between diet group and test time was significant, F (1, 23) = 8.16, p = .009, η^2 = .26. However, the follow up dependent t-tests did not show a significant difference in fat preference for the HF group from test time #1 (M = .13, SD = .10) to test time #2 (M = .21, SD = .13), t(12) = -2.50, p = .062, or for the LF group from test time #1 (M = .26, SD = .12) to test time #2 (M = .18, SD = .11), t(11) = 1.99, p = .072. Except for the significant interaction during the 0-30 minute time period, fat preference by the high dose was not significantly affected by diet group, test time, or a combination of the two during all other time periods.

HF group.

To determine the differences in effectiveness of quinpirole on the dietary manipulation of the HF group, a separate one way repeated measures ANOVA for drug test #1 and drug test #2 was used to analyze the vehicle, low, medium, and high dose (within factor) during the 0-180 time period. Significant main effects were followed by two-tailed dependent measures t-tests. All means and standard deviations are shown in Table 12 and 22.

There was a significant main effect for drug dose during the 0-180 minute time period at drug test #1 in the HF group, F (3, 36) = 9.77, p < .001, η^2 = .45. Fat preference

was significantly decreased at the high dose compared to the medium dose, $t(12) = 3.52$, $p = .004$, $d = .80$, low dose, $t(12) = 2.99$, $p = .011$, $d = 1.23$, and vehicle, $t(12) = 5.37$, $p < .001$, $d = .1.73$. The medium dose significantly decreased fat preference compared to the vehicle, $t(12) = 3.04$, $p = .010$, $d = .88$, but not the low dose, $t(12) = .88$, $p = .394$. There was not a difference in fat preference at the low dose compared to vehicle, $t(12) = 2.00$, $p = .069$. Although fat preference had a dose dependent decrease, quinpirole was most effective at the high dose compared to all other doses, and at the medium dose compared to vehicle at drug test #1.

Drug dose produced a significant main effect on fat preference during the 0-180 minute time period at drug test #2, $F(3, 36) = 11.41$, $p < .001$, $\eta^2 = .49$. The high dose significantly decreased fat preference compared to the medium dose, $t(12) = 2.69$, $p = .020$, $d = 1.02$, low dose, $t(12) = 4.08$, $p = .002$, $d = .95$, and vehicle, $t(12) = 4.86$, $p < .001$, $d = 1.87$. Fat preference at the medium dose was significantly lower than at vehicle, $t(12) = 5.06$, $p < .001$, $d = 1.27$, but not the low dose, $t(12) = .72$, $p = .485$. The low dose significantly lowered fat preference compared to the vehicle, $t(12) = 1.75$, $p = .105$, $d = .63$. Interestingly, fat preference at the medium dose was slightly higher than at the low dose, whereas it was lower at the medium dose in drug test #1. However, there was not a significant difference between the medium and low dose in either drug test. The high dose proved to be the most effective at decreasing fat preference in the HF group during drug test #2.

Energy Intake.

Twenty-four Hour Intake Test and Baseline.

Intake Percentage.

After noting the excessive energy intake of the LF group during baseline #1, and both groups during baseline #2, a new dependent variable was developed to examine the difference between the calories consumed during baseline and the regular daily intake. Intake percentage is the amount of energy intake (total calories/ kg body weight) consumed during a time period at baseline divided by the amount of energy intake consumed during the corresponding 24 hour intake test. The 24 hour intake test was conducted the week prior to testing at both test times, and only included the maintenance diet, while the baseline included both diets.

A two-tailed independent measures t-test was used to look for differences in energy intake between the diet groups during the 24 hour intake test during test time #1. The HF group ($M = 212.2$, $SD = 17.2$) had a similar amount of energy intake as the LF group ($M = 213.8$, $SD = 12.9$), $t(23) = .26$, $p = .798$. A two-tailed independent measures t-test analyzed the differences in the 0-30 minute intake percentage between the diet groups. The LF group consumed 21.6% ($SD = 5.2$) of their average daily intake in the first 30 minutes of the baseline fat preference test, which was significantly more than the 16.5% ($SD = 4.5$) that the HF group consumed, $t(23) = .26$, $p = .015$, $d = 1.05$. Refer to Figure 7 for an overview of the of intake percentage for the HF and LF groups. The LF group consumed 48.2 % ($SD = 13.7$) of their daily intake in the first 120 minutes of baseline, which was significantly more than the 28.5 % ($SD = 7.7$) that the HF group

consumed (SD = 17.2), $t(23) = .26$, $p = .015$, $d = 1.05$. For the overall (0-180 minutes) intake percentage, the LF group consumed 75.6% (SD = 13.3) of their daily average energy intake, which was again significantly more than the 37.6% (SD = 5.4) the HF group consumed, $t(23) = 9.49$, $p < .001$, $d = 3.74$. Even though the HF and LF group consumed a similar amount of calories prior to baseline preference testing, the LF group consumed significantly more than the HF group during testing.

Energy intake during test time #2 proved to be the opposite of test time #1. The LF group (M = 191.1, SD = 11.1) had a significantly higher amount of energy intake compared to the HF group (M = 178.7, SD = 8.7) during the 24 hour intake test during test time #2, $t(23) = 3.14$, $p = .005$, $d = 1.24$. The LF group consumed 32.9% (SD = 13.7) of their energy intake during the first 30 minutes of baseline #2, which was not significantly different from the 37.9% (SD = 12.1) that the HF group consumed, $t(23) = -.95$, $p = .351$. During the first 120 minutes, there was no difference between in intake percentage between the 61.3% (SD = 13.1) the LF group consumed and the 57.1% (SD = 15.1) the HF group consumed, $t(23) = .73$, $p = .470$. For overall baseline #2, the LF group consumed 75.6% (SD = 13.7) of their daily energy intake, which was not significantly different from the HF group that consumed 69.3% (SD = 18.2), $t(23) = .90$, $p = .378$. The HF group consumed significantly less of the low fat diet during the 24 hour intake compared to the LF group, but both groups had similar patterns of consumption during the baseline preference test.

A two way (2 X 2) mixed ANOVA was used to analyze differences in the percentage of energy intake during the 0-30, 0-120, and 0-180 minute time period for the

HF and LF group (between factor) from baseline #1 to baseline #2 (within factor). Significant interactions were followed up with dependent measures t-tests.

There was not a significant difference in the percentage of energy intake between the HF (M = 27.2, SD = 8.3) and LF (M = 27.3, SD = 9.5) group during the first 30 minutes, F (1, 23) = .00, p = .975, η^2 = .00. There was a significant main effect for baseline testing time, where intake percentage was significantly higher in Baseline #2 (M = 35.5, SD = 12.9) compared to Baseline #1 (M = 18.9, SD = 5.4), F (1, 23) = 39.21, p < .001, η^2 = .63. Refer to Figure 8 for overview. The interaction between diet group and baseline testing time was not significant, F (1, 23) = .3.67, p = .068, η^2 = .14. The HF and LF group did not differ in the intake percentage over both baselines, but the two groups combined consumed a significantly higher percentage of their 24 hour intake in the first 30 minutes of baseline #2 compared to baseline #1.

The LF group (M = 54.8, SD = 13.4) had a significantly higher intake percentage than the HF group (M = 42.8, SD = 11.4) during the 0-120 minute time period, in which the main effect was significant, F (1, 23) = 8.46, p = .008, η^2 = .27. There was a significant main effect for baseline testing time, and intake percentage was significantly higher at baseline #2 (M = 59.1, SD = 14.0) compared to baseline #1(M = 38.0, SD = 14.7), F (1, 23) = 48.25, p < .001, η^2 = .68. The interaction between diet group and baseline testing time was significant, F (1, 23) = 6.68, p = .017, η^2 = .23. Both the HF and the LF group had a significant increase in intake percentage from baseline #1 to baseline #2, t(12) = -8.37, p < .001, d = 2.39 and t(11) = 2.60, p = .025, d = .98, respectively. The LF group consumed more during the 0-120 time period at both baselines, and both groups

together and separately consumed more during baseline #2 compared to baseline #1.

There was a significant main effect for diet group, in which the LF group (M = 75.4, SD = 13.5) had a significantly higher intake percentage than the HF group (M = 53.5, SD = 11.8), $F(1, 23) = 24.28$, $p < .001$, $\eta^2 = .51$. Baseline #2 (M = 72.1, SD = 16.2) had a significantly higher percentage than baseline #1 (M = 55.8, SD = 21.7), and the main effect was significant, $F(1, 23) = 26.34$, $p < .001$, $\eta^2 = 53$. There was also a significant interaction between diet group and baseline testing time, $F(1, 23) = 27.67$, $p < .001$, $\eta^2 = .55$. There was a significant increase in energy intake percentage for the HF group from baseline #1 to baseline #2, $t(12) = -6.82$, $p < .001$, $d = 2.36$, but there was not a difference for the LF group, $t(11) = .10$, $p = .921$. Overall, there was very little change in the energy intake consumption for the LF group from baseline #1 to baseline #2, however, there was a significant increase in energy intake consumption for the HF group from baseline #1 to baseline #2.

Discussion

The results of the current research demonstrate the efficacy of the dopamine D_2/D_3 agonist, quinpirole, in decreasing preference for high fat foods and overall energy intake in rats that are maintained on both a high and low fat diet. Quinpirole was effective in a dose dependent manner at test times #1 and #2. The current research also found that being maintained on a high fat diet decreases energy intake and fat preference at some time periods during a preference test. However, there are few differences in energy intake and no differences in fat preference after a switch to a low fat diet. Overall, the amount of fat in a maintenance diet and the neurotransmitter dopamine definitely impact high fat food preference.

In a previous study using the same high fat diet that was used in the current study, rats maintained on the diet for 45 days gained significantly more weight than chow fed control rats (Wellman et al., 2007). This was not the case in the current experiment as the high fat diet did not cause a significant difference in body weights between the HF and LF groups. While the HF group did weigh more than the LF group at baseline #1, it was not significantly more. This is a curious result because all of the HF rats readily approached and consumed the high fat diet as it was placed in their cage every day. Although the HF rats weighed slightly less than the LF rats during the first week of the experiment, they subsequently gained weight and weighed more than the LF rats every week after that, until mid-way through test time #2. After the diet switch, the HF group did not gain as much weight as the LF group throughout the rest of the study. Overall, the

fact that there were no differences in the weights of both groups makes the differences in energy intake and fat preference even more intriguing, in that the differences can be attributed solely to the diet and drug dose.

Since food preferences can develop through familiarity and consumption (Birch, 1999), it was hypothesized that at baseline #1 and #2, the rats in the HF group would have a significantly greater preference for high fat food and greater total intake than rats in the LF group. However, the LF group had significantly higher energy intake than the HF group at all time periods during baseline #1, but their preferences for high fat food were equal. Also, energy intake during a 24 hour intake test at the beginning of test time #1 was equal for both groups (calories/kg body weight). These results are in accordance with many binge eating studies that focus on limited access to palatable food. Binges consist of eating large quantities of (usually palatable) food within a discrete amount of time, typically within 2 hours (Corwin & Buda-Levin, 2004). A previous study found that intermittent restricted access to shortening resulted in binge-like behavior in rats compared to rats with regular access for six weeks (Corwin et al., 1998). The intermittent rats consumed 51% of a control group's 24 hour intake within 2 hours of access to shortening, while the regular rats only consumed 32%. In the current study, during the first 2 hours of baseline #1, the LF group (which only had limited access to the HF diet similar to the rats described above) consumed 48.2% of their daily intake, which was significantly more than the 28.5% the HF group consumed. One difference in these studies is that the present study included high and low fat diets while the Corwin et al. study used only shortening. Further supporting the concept of binge eating, during all 3

hours of baseline #1, the LF group consumed 75.6% of their daily intake, which is double the 37.6 % consumed by the HF group.

Similar results were found by Wojnicki, Johnson, and Corwin (1999) where rats were given unlimited access to vegetable shortening and chow while control rats had only chow. After five weeks, the unlimited access group was split and half were given access to shortening one hour every day while the other half had intermittent shortening access for an additional five weeks (5-10). The chow fed control rats were also put on the intermittent access schedule. The control rats ate significantly more shortening than any other group during every week of shortening access (weeks 5-10). This same result has also been found in children where limiting the access of a previously neutral food caused the children to eat significantly more of the food during a five minute access period compared to a freely available food (Fisher & Birch, 1999). Overall, the HF group, which had unrestricted access to the high fat diet, did not binge during the preference test, while the LF group did, consuming twice as much of their daily intake compared to HF rats.

However, this pattern of results changed at test time #2, during which the HF group was put on a low fat diet for six weeks. Interestingly, fat preference was significantly higher in the LF group during the 30-60 and 60-120 minute intervals compared to the HF group during baseline #2. This occurred despite energy intake being the same between the two groups at all time periods. Overall, hypothesis #2 was not supported. Further, energy intake of the LF group during the 24 hour intake test at test time #2 was significantly greater than of the HF group. But, during the first 2 hours at baseline #2 the LF group consumed 61.3 % of their average daily intake and the HF

group consumed 57.1 %, indicating a lack of difference in bingeing behavior. The same was true for all 3 hours of baseline where the LF group consumed 75.2% of their daily energy intake, which was not significantly different from the HF group which consumed 69.3%. Further analysis of an interaction (diet group by baseline test time) at 180 minutes found that HF rats' intake had significantly increased from test time #1 to test time #2, but there was not a similar change for the LF group.

This change in intake behavior for the HF group is can be interpreted in the context of a negative contrast effect, in which a shift from a large to a small reward results in a decrease in behavior (Rogers, 1985). This implies that the rats ate significantly less of the plain chow diet (small reward) after being maintained on a palatable high fat diet (large reward). In Rogers' study, rats were given an unrestricted cafeteria style diet while control rats were given chow for 48 days. All rats were switched to chow and the unrestricted cafeteria style diet rats ate significantly less than the control rats for the entire 30 days of chow. The unrestricted cafeteria style diet rats weighed significantly more than the control rats at the start of the chow period, but after 30 days the weights were no longer significantly different. There also exists a positive contrast effect, where rats will eat significantly more of a palatable food after being maintained on chow (Davies et al., 2006). The positive and negative contrast effects were apparent in the Rossi et al. (1997) study where rats consumed significantly more food after being switched from a low fat diet to a high fat diet, but then significantly decreased consumption when they were switched back to the low fat diet. These contrast effect help explain why the LF group ate so much food at both test times (positive contrast as no

exposure to high fat diet) and the HF group matched the intake of the LF group at test time #2 (positive contrast for high fat diet after 6 weeks of low fat diet only). The current results also agree with previous literature which stated that a significant preference for a high fat diet will continue even after a diet change to a low fat diet (Mattes, 1993; Reed et al., 1992; Teegarden et al., 2009; Warwick et al., 1990).

Dopamine may also play a role in the persistent preference for the HF diet, because long term exposure to a high fat diet significantly reduces the dopamine response to eating a low fat food, but elicits a significant increase in response to eating a high fat food (Geiger et al., 2009). Some studies have shown that these dopamine levels will start to rebound with a change to a low fat diet (like the diet switch for the HF group in the current study), and others have shown dopamine agonists decrease consumption of low and high fat foods (Cooper & Al-Naser, 2006; Kaur & Kulkarni, 2002; McQuade et al., 2003; South & Huang, 2008). In the current study, quinpirole, a D_2/D_3 agonist, successfully decreased consumption of both low and high fat foods in both the HF and LF groups at both test times #1 and #2, which is in agreement with these previous studies.

The third hypothesis was partially supported by the high and medium dose of quinpirole producing a significant dose-dependent decrease in energy intake for both diet groups at test time #1. Overall, the low dose was effective at decreasing fat preference in both groups combined during only the 0-30 and 0-120 minute time period. The medium dose decreased interval intake during the 0-30, 60-120 and cumulative intake during the 0-60, 0-120, and 0-180 time periods. The high dose proved to be the most effective by decreasing energy intake during all of the time periods. In addition, the medium and high

doses effectively decreased energy intake in the HF group during the 0-120 and 0-180 minute time period while only the medium dose was effective during the 60-120 minute time period. For the LF group, the medium and high dose significantly decreased energy intake during the 30-60 minute interval and cumulatively during the 0-120, and 0-180 time periods, and only the high dose decreased energy intake (interval) from 60-120 minutes. Thus, while the low dose decreased energy intake during two cumulative time periods, the medium dose was effective at most of the time periods, and the high dose was effective at all time periods during test time #1.

During test time #2, quinpirole was more effective at significantly decreasing energy intake in both diet groups combined. A main effect showed that all doses significantly decreased energy intake during the 30-60 (interval), 0-60, 0-120, and 0-180 (cumulative) minute time periods. The medium and high doses were also effective during the 0-30 minute time period, while only the high dose was effective during the 120-180 minute time period. Although the low dose did not decrease energy intake from 0-30 minutes as it did at test time #1, it was effective during the subsequent time interval and all other cumulative time periods. At test time #1, the medium dose significantly decreased energy intake during the 60-120 minute time period, while it decreased energy intake during the time interval prior (30-60) at test time #2. Although the high dose remained the most effective dose at decreasing energy intake, it did not affect energy intake during the 60-120 minute time period. In examining the only diet group by drug dose interaction, during the 0-180 minute time period energy intake in the HF group was significantly decreased by the high, medium, and low doses, while energy intake in the

LF group was only decreased by the high and medium doses. Overall, the low dose's efficacy at decreasing energy intake in both groups combined and during the 0-180 minute time period for the HF group during test time #2 is likely due to the diet change, as it had little impact on energy intake in test time #1. The medium dose was equally effective at both test times, while the high dose was ineffective at decreasing energy intake during only one time interval during test time #2. Therefore, the medium and high doses of quinpirole significantly decrease energy intake in rats maintained on only a high fat or low fat diet, however a diet switch from a high to low fat diet made the low dose more effective with only minor changes in the effectiveness of the medium and high doses. These results also support the third hypothesis in that quinpirole did produce a significant dose dependent decrease in overall energy intake in both diet groups.

These results are favorable to the efficacy of quinpirole, given that the LF group had significantly higher energy intake compared to the HF group during every time period at test time #1, and during the 0-30, 30-60, 0-60, and 0-120 minute periods at test time #2. Thus, even excessive intake (such as bingeing) of high fat food can be decreased by the medium and especially the high doses of quinpirole.

Hypothesis #4 states that at test times #1 and #2, quinpirole will produce a significant dose-dependent decrease in overall high fat food preference in the HF group. In this group, fat preference was significantly decreased by only the high and medium doses of quinpirole during the 0-180 time period at test time #1. However, during the 0-180 minute time period at test time #2, fat preference was significantly decreased by the high, medium, and low doses, but there was not a difference between the medium and

low doses. There is a possibility that the increased effects of quinpirole at test time #2 are due to a rebound in the level of dopamine response to food after 6 weeks of a low fat diet, however this seems unlikely since the low dose was not especially effective in only the LF group. A more likely explanation is related to the switch from a high fat to a low fat diet. This, as discussed above, could result in a rebound in the dopamine response to food that, in combination with a low dose of a dopamine agonist and access to both diets during the drug testing period, leads to a decrease in overall fat preference for the HF group. Therefore, hypothesis #4 was supported at test times #1 and #2.

Related to this hypothesis, but not initially part of its focus, quinpirole produced a significant dose-dependent decrease during most time periods in high fat food preference for both groups combined at both test times. During test time #1, the high dose significantly decreased fat preference during the 0-30, 30-60, 60-120 (intervals), 0-60, 0-120, and 0-180 (cumulative) time periods, but not the 120-180 minute interval. The low and medium doses effectively decreased fat preference during from 0-60 and 0-120 minutes, and the medium dose was also effective from 0-180 minutes. The only diet group by dose interaction in fat preference occurred during the 30-60 minute interval, and this was due to the high dose significantly decreasing fat preference in only the LF group. The high dose proved to be most effective dose in decreasing fat preference during test time #1.

During test time #2, fat preference was significantly decreased by the high, medium, and low dose of quinpirole during the 0-30, 30-60, 0-60, 0-120, and 0-180 minute time periods, and only the high dose during the 120-180 minute time period. Fat

preference was unaffected by quinpirole during the 60-120 minute time period during test time #2, as was energy intake also. The high dose, once again, proved to be the most successful at decreasing fat preference during test time #2, but was equally effective compared to test time #1. Overall, all doses of quinpirole were successful at decreasing fat preference during all cumulative time periods and half of the interval time periods. These results are likely driven by the HF group being switched from the high to low fat diet as discussed in connection with hypothesis #4.

The final hypothesis stated that the dose-dependent effects of quinpirole on high fat food preference will be significantly less at test time #2 versus test time #1 in the HF group as compared to the LF group. Interestingly, fat preference in both groups combined at test time #2 was significantly higher than test time #1 in most cumulative time periods for vehicle, low, and medium doses (see Table 26 and 27). However, following the high dose there were no significant differences between the diet groups in fat preference at test times #1 and #2. There was an interaction during the 0-120 and 0-180 time periods for the medium dose in that, in support of the hypothesis, the HF group significantly increased fat preference from test time #1 to test time #2, while there was no significant difference in the LF group. The high dose had different results than the rest of the doses and did not produce any significant differences between the groups or from test time #1 to test time #2. There was a significant interaction, in which the HF group increased fat preference and the LF group decreased fat preference from test time #1 to test time #2, but neither change was significant. Results from the medium and high doses provide

partial support to the hypothesis. Overall, high fat food preference increased in the HF group from test time #1 to test time #2 for all doses of quinpirole.

Overall, the ability of the high dose to decrease both energy intake and fat preference could result from quinpirole having a biphasic effect on locomotion and movement (Eilam & Szechtman, 1989). A low dose of quinpirole (< 0.1 mg/kg) activates presynaptic receptors and reduces locomotion, while a high dose (> 0.1mg/kg) activates pre and postsynaptic receptors and has a brief period of inhibition on locomotion, followed by hyperactivity (Cory-Slechta, Zuch, & Fox, 1996). Therefore, the possibility exists that the high dose (.1mg/kg) was more successful than the low (.01 mg/kg) and medium (.05 mg/kg) doses because it activated both post- and presynaptic receptors. However, all rats consumed either high or low fat food within the first 30 minutes of the drug tests, except for one LF rat during test time #2 that started consuming food during the 30-60 minute interval after administration of the high dose. Also, for rats receiving the high dose at the beginning of the first two counterbalanced drug tests, there appeared to be some motor suppression (not directly measured), but the high dose was indistinguishable from the third test through the end of the experiment. Other research also found that a low and high dose (0.03 and 0.1mg/kg) dose dependently decreased the amount of palatable food consumed and increased the amount of regular maintenance chow consumed, all while it decreased the total amount of food consumed without interfering in the initiation of feeding (Cooper & Al-Naser, 2006).

Future Research

There are several possibilities for future endeavors in the long term high fat preference paradigm. One is using a more palatable high fat diet, such as a cafeteria style diet or chocolate-coated biscuits (Cooper & Al-Naser, 2006; Sclafani & Springer, 1976) to make the diet more similar to what people currently choose as high fat foods and therefore give the pharmacological intervention higher external validity. In addition, maintaining the HF group on the high fat diet for more than 8 weeks could lead to significantly greater body weight compared to rats fed the LF diet, as has been previously reported (Davis et al., 2008; Sclafani & Springer, 1976).

During the preference tests, food consistency may also be a factor as the low fat chow pellets were hard and the high fat diet had a mushy consistency. One possibility would be to use high fat pellets and low fat pellets, or low fat ground chow with an emulsifier to match the consistency of the high fat mixture (Teegarden et al., 2009; Warwick et al., 1990). Another possibility is to use a completely different food such as peanut butter with different amounts of oil added, so that the peanut butter would be novel to both groups (Warwick et al., 1990). Alternatively, the high fat preference test could be a high fat conditioned place preference test, which has been used to assess how food cues elicit "cravings" for food (Sobik, Hutchison, & Craighead, 2005). Conditioned place preference tests are effectively used in drug abuse studies, and in high fat and high sugar food studies with drug interventions (Jarosz, Sekhon, & Coscina, 2006).

Additionally, many of the animal studies using pharmaceutical interventions only give the animals a high fat diet for a short period of time (e.g. 2-4 weeks) (Cooper & Al-

Naser, 2006; McQuade et al. 2003). However, as a high fat diet is a way of life for many people, the present study attempted to extend previous findings with longer-term high fat exposure in order to investigate potential long term neurochemical changes not revealed in other studies. The present results were similar to those of previous studies in that quinpirole produced a dose-dependent reduction in high fat intake. Taken together, these results imply that exposure to a high-fat food, whether short- or long-term, results in a dopamine signaling system that responds similarly to pharmacological manipulations (dopamine agonists). Further, this responsiveness is retained even after a prolonged (6-week) break from the high-fat food. Repercussions of this exposure, then, could impact food choice throughout life.

Regardless of which of the procedural adjustments discussed above were implemented, as this paradigm is unique in its exposure/switching framework, the impact of other dopaminergic compounds (including 7-OH-DPAT, bromocriptine, and apomorphine) merits investigation. While these drugs have been shown to decrease intake, (Davis et al., 2009; Kuo, 2002; McQuade et al. 2003), they have been tested in other ingestion paradigms.

The current research has some intriguing findings. The unlimited availability of the high fat food during test time #1 for the HF group seemed to prevent them from engaging in a binge-like behavior, whereas the LF group, which only had limited availability of high fat food, did binge during the preference test. However, after the HF group was switched to a low fat diet, they had similar energy intake and fat preference as the LF group during the preference tests – i.e. both groups binged. The has implications

for bingeing in humans, who, despite making healthy dietary choices for a long period of time, when presented with high-fat foods, may not be able to resist making unhealthy choices: consuming a large amount of high fat food in a relatively short period of time.

Despite the behavioral differences noted above, at both test times, the impact of quinpirole was similar. In this test time #1, the medium and high doses decreased both energy intake and fat preference in both groups of rats, while at test time #2 all three doses produced decreases in energy intake and fat preference. This discrepancy between the behavioral and drug responses remains to be fully explained. It is possible that the familiarization sessions, during which the bingeing was evident (and it was present during baseline and vehicle conditions), produced effects on the dopamine signaling systems in both diet groups that made them equally responsive to the impact of quinpirole. Adjustments to the degree (number or length) of familiarization may address this possibility.

One positive finding is that the HF group never significantly exceeded the energy intake or fat preference of the LF group at test time #2. Therefore, being initially maintained on a high fat diet and subsequently switching to a low fat diet can lead to food preferences that mimic those resulting from consistent exposure to only a low fat diet, even when presented with a high-fat choice. Extending this concept to humans, many of the negative health effects of prolonged exposure to unhealthy food (whether early in development or later: the rats in the current study were adults) may be reversible through dietary modification. In cases where this modification is ineffective, pharmacological manipulation of the dopamine system (based on the results of all doses of the D_2/D_3

agonist used here) may help to decrease energy intake and fat preference, thus resulting in greater appetite control, subsequent weight loss and overall health benefits.

Table 1

Schedule of phases with corresponding test times and diet.

Phase	Time Frame	LF Group	HF Group
Diet Exposure & 24 Hour Intake	Weeks 1-8	LF group maintained on low fat diet	HF group maintained on high fat diet
Familiarization & Baseline #1	Week 9	3 consecutive familiarization trials and baseline taste preference test	
Drug Test #1	Weeks 9-10	4 taste preference tests with different doses of quinpirole conducted every 72 hours	
Diet Switch & 24 Hour Intake	Weeks 11-16	LF group maintained on low fat diet	HF group switched to low fat diet
Familiarization & Baseline #2	Week 17	3 consecutive familiarization trials and baseline taste preference test	
Drug Test #2	Week 17-18	4 taste preference tests with different doses of quinpirole conducted every 72 hours	

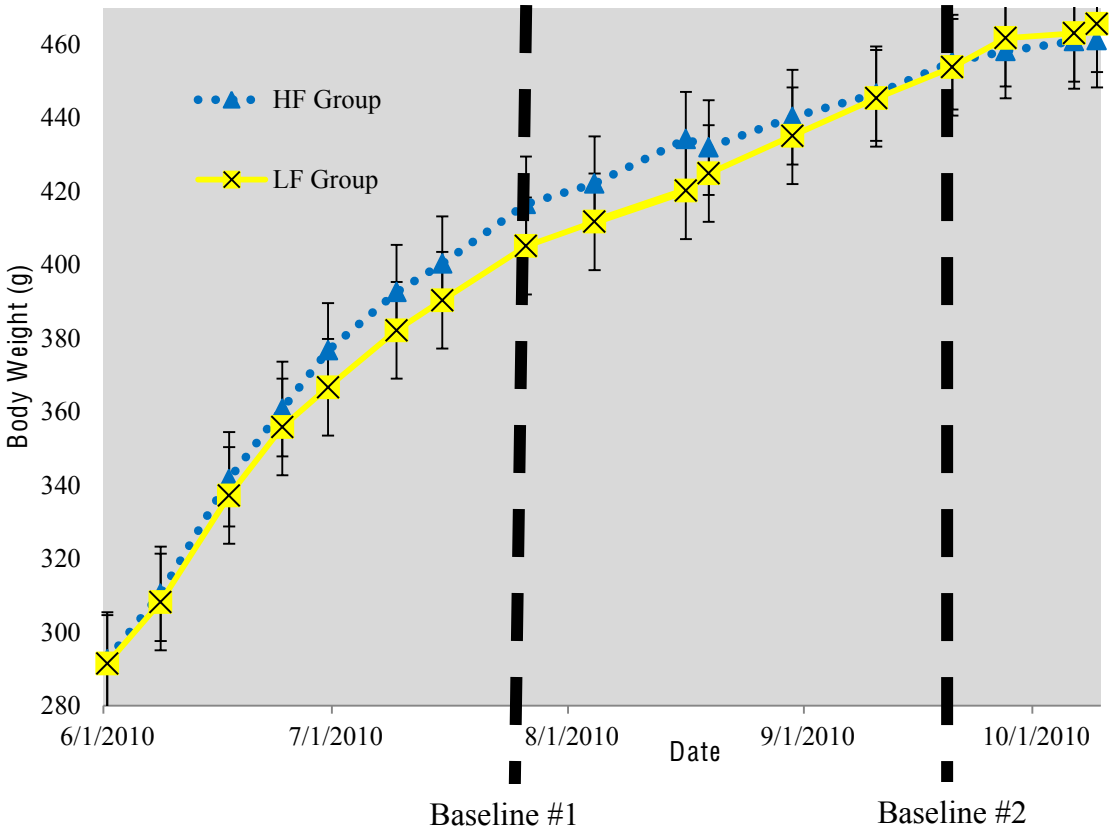

Figure 1. Body weights (grams) of HF and LF groups throughout the experiment. Every third body weight that was recorded is shown. LF group had a significant difference in body weight from Baseline #1 to Baseline #2, from Baseline #1 to the end of the experiment, and from Baseline #2 to the end of the experiment. The HF Group had a significant difference in body weight from Baseline # 1 to Baseline #2 and from Baseline #1 to the end of the experiment, but not from Baseline #2 to the end of the experiment, $p < .001$. Error bars represent +/- 1 SE.

Table 2

Statistical analyses for all dependent variables.

Dependent Variable	Statistical Analysis
Weight	Two way (2 X 3) mixed ANOVA
	Main Effect- two-tailed dependent measures t-test
	Interaction- repeated measures ANOVA
	Followed by two-tailed dependent measures t-test
Test Time #1	
Energy Intake	
Baseline	Two-tailed independent samples t-test
Baseline vs Vehicle	Two-tailed dependent measures t-test
Drug Test	
0-30 minutes	Two way (2 X 5) mixed ANOVA
All Other Times	Two way (2 X 4) mixed ANOVA
	Main Effect- two-tailed dependent measures t-test
	Interaction- repeated measures ANOVA
	Followed by two-tailed dependent measures t-test
Fat Preference	
Baseline	Two-tailed independent samples t-test
Baseline vs Vehicle	Two-tailed dependent measures t-test
Drug Test	
0-120 minutes	Two way (2 X 5) mixed ANOVA
All Other Times	Two way (2 X 4) mixed ANOVA
	Main Effect- two-tailed dependent measures t-test
	Interaction- repeated measures ANOVA
	Followed by two-tailed dependent measures t-test
Test Time #2	
Energy Intake	
Baseline	Two-tailed independent samples t-test
Baseline vs. Vehicle	Two-tailed dependent measures t-test
Drug Test	Two way (2 X 4) mixed ANOVA
	Main Effect- two-tailed dependent measures t-test
	Interaction- repeated measures ANOVA
	Followed by two-tailed dependent measures t-test
Fat Preference	
Baseline	Two-tailed independent samples t-test
Baseline vs. Vehicle	Two-tailed dependent measures t-test
Drug Test	
0-30 and 0-180	Two way (2 X 5) mixed ANOVA
All Other Times	Two way (2 X 4) mixed ANOVA
	Main Effect- two-tailed dependent measures t-test
	Interaction- repeated measures ANOVA
	Followed by two-tailed dependent measures t-test

Table 2 continued.
Statistical analyses for all dependent variables.

Dependent Variable	Statistical Analysis
Test Time #1 vs. Test Time #2	
Fat Preference	Two way (2 X 2) mixed ANOVA
	Interaction- repeated measures ANOVA
	Followed by two-tailed dependent measures t-test
HF Group	One way repeated measures ANOVA
	Main Effect- two-tailed dependent measures t-test
Intake Percentage	
24 hour Intake	Two-tailed independent samples t-test
0-30, 0-120, and	Two way (2 X 2) mixed ANOVA
0-180	Interaction- repeated measures ANOVA
	Followed by two-tailed dependent measures t-test

Table 3

Mean (SD) of Energy Intake *for both diet groups and all drug doses for interval test periods at Test Time #1.*

0-30 minutes

Diet Group	Baseline	Vehicle (0)	Low (.01)	Medium (.05)	High (.1)
LF Group	46.2 (11.8)	70.2 (29.2)	53.5 (15.0)	45.6 (10.2)	39.5 (17.2)
HF Group	35.1 (10.6)	39.2 (23.2)	30.4 (16.0)	26.0 (10.7)	22.0 (7.7)
Total	40.4 (12.4)	54.1 (30.1)	41.5 (19.2)	35.4 (14.3)	30.4 (15.6)

30-60 minutes

LF Group	27.7 (18.6)	20.0 (14.5)	25.0 (12.9)	10.7 (13.0)	11.1 (9.6)
HF Group	8.7 (7.7)	7.1 (6.4)	5.2 (4.9)	7.0 (7.0)	4.0 (3.1)
Total	17.8 (16.8)	13.3 (12.7)	14.7 (13.8)	8.8 (10.3)	7.4 (7.8)

60-120 minutes

LF Group	29.2 (25.7)	45.1 (25.3)	34.9 (17.9)	24.8 (19.0)	14.1 (8.2)
HF Group	17.1 (12.7)	17.6 (10.3)	15.1 (10.8)	7.1 (6.5)	10.2 (7.3)
Total	22.9 (20.5)	30.8 (23.3)	24.6 (17.5)	15.6 (16.4)	12.1 (7.8)

120-180 minutes

LF Group	59.0 (22.1)	45.2 (24.7)	50.2 (23.4)	52.9 (30.8)	31.4 (13.8)
HF Group	18.9 (10.3)	17.5 (12.0)	16.9 (12.4)	22.3 (12.5)	12.5 (6.1)
Total	38.2 (26.4)	30.8 (24.5)	32.9 (24.8)	37.0 (27.5)	21.6 (14.1)

Table 4

Mean (SD) of Energy Intake *for both diet groups and all drug doses for all cumulative test periods at Test Time #1.*

Diet Group	Baseline	Vehicle (0)	Low (.01)	Medium (.05)	High (.1)
0-30 minutes					
LF Group	46.2 (11.8)	70.2 (29.2)	53.5 (15.0)	45.6 (10.2)	39.5 (17.2)
HF Group	35.1 (10.6)	39.2 (23.2)	30.4 (16.0)	26.0 (10.7)	22.0 (7.7)
Total	40.4 (12.4)	54.1 (30.1)	41.5 (19.2)	35.4 (14.3)	30.4 (15.6)
0-60 minutes					
LF Group	73.9 (22.9)	90.3 (37.8)	78.5 (17.8)	56.3 (17.6)	50.6 (17.3)
HF Group	43.8 (13.0)	46.3 (24.3)	35.6 (15.2)	33.0 (10.6)	26.0 (6.2)
Total	58.3 (23.7)	67.4 (38.1)	56.1 (27.2)	44.2 (18.4)	37.8 (17.7)
0-120 minutes					
LF Group	103.1 (29.7)	135.4 (49.9)	113.3 (24.0)	81.1 (18.5)	64.7 (15.4)
HF Group	60.9 (18.7)	63.8 (22.7)	50.7 (15.6)	40.1 (13.0)	36.2 (10.7)
Total	81.2 (32.3)	98.2 (52.3)	80.7 (37.5)	59.8 (26.1)	49.9 (19.4)
0-180 minutes					
LF Group	162.1 (33.0)	180.6 (56.9)	163.5 (41.0)	134.0 (34.5)	96.1 (21.7)
HF Group	79.8 (13.9)	81.3 (27.8)	67.6 (16.0)	62.3 (20.1)	48.7 (8.9)
Total	119.3 (48.5)	128.9 (66.6)	113.6 (57.3)	96.7 (45.6)	71.5 (29.0)

Table 5

Independent measures t-tests between the HF and LF groups at all time periods for Energy Intake *at Baseline #1.*

Time Interval	*df*	*t*	*p*	*d*
0-30	23	2.48	.021	.99
30-60	14.4	3.29	.005	1.34
60-120	15.8	1.47	.162	.60
120-180	15.3	5.73	.000	2.33
Time Cumulative				
0-30	23	2.48	.021	.99
0-60	23	4.08	.000	1.61
0-120	23	4.28	.000	1.70
0-180	23	8.01	.000	3.25

Note. **Bold type** indicates the HF group had significantly lower energy intake, $p < .05$.

Table 6

Dependent measures t-tests on the amount of Energy Intake *for the HF and LF groups combined at Baseline #1 compared to vehicle at all time periods.*

Time Interval	*df*	*t*	*p*	*d*
0-30	**24**	**-2.49**	**.020**	**.60**
30-60	24	1.29	.208	.30
60-120	24	-1.59	.126	.36
120-180	24	1.41	.170	.30
Time Cumulative				
0-30	**24**	**-2.49**	**.020**	**.60**
0-60	24	-1.55	.135	.29
0-120	24	-2.02	.055	.39
0-180	24	-1.28	.214	.17

Note. **Bold type** indicates energy intake with vehicle was significantly higher than baseline, $p < .05$.

Table 7

T score, p value and Cohen's d value results for dependent measures t-test on Energy Intake *at Test Time #1 during 30-60 minutes for both groups and for the LF group.*

	Vehicle (0)	Low (.01)	Medium (.05)
Low. *t (df)*	-.51 (24)		
p (*d*)	.615		
Medium. *t (df)*	1.40 (24)	1.91 (24)	
p (*d*)	.174	.068	
High. *t (df)*	**2.52 (24)**	**3.26 (24)**	.64 (24)
p (*d*)	**.019 (.55)**	**.003 (.66)**	.529

LF Group	Vehicle	Low	Medium
Low. *t (df)*	-.90 (11)		
p (*d*)	.388		
Medium. *t (df)*	1.52 (11)	**2.84 (11)**	
p (*d*)	.158	**.016 (1.10)**	
High. *t (df)*	1.99 (11)	**3.79 (11)**	-.11 (11)
p (*d*)	.071	**.003 (1.22)**	.916

Note. **Bold type** indicates significance at $p < .05$.

Table 8

T score, p value and Cohen's d value results for dependent measures t-test on Energy Intake *at Test Time #1 during 60-120 minutes for both groups followed by LF and then HF group.*

	Vehicle	Low	Medium
Low. *t (df)*	1.46 (24)		
p (*d*)	.158		
Medium. *t (df)*	**3.10 (24)**	**2.18 (24)**	
p (*d*)	**.005 (.75)**	**.040 (.53)**	
High. *t (df)*	**3.89 (24)**	**3.97 (24)**	1.07 (24)
p (*d*)	**.001 (1.07)**	**.001 (.92)**	.294
LF Group			
Low. *t (df)*	1.20 (11)		
p (*d*)	.255		
Medium. *t (df)*	2.17 (11)	1.31 (11)	
p (*d*)	.053	.218	
High. *t (df)*	**3.86 (11)**	**4.23 (11)**	1.90 (11)
p (*d*)	**.003 (1.65)**	**.001 (1.49)**	.084
HF Group			
Low. *t (df)*	1.05 (12)		
p (*d*)	.316		
Medium. *t (df)*	**2.77 (12)**	2.05 (12)	
p (*d*)	**.017 (1.22)**	.063	
High. *t (df)*	2.11 (12)	1.75 (12)	-1.20 (12)
p (*d*)	.057	.105	.255

Note. **Bold type** indicates significance at $p < .05$.

Table 9

T score, p value and Cohen's d value results for dependent measures t-test on Energy Intake *at Test Time #1 during 0-120 minutes for both groups followed by LF and then HF group.*

	Vehicle	Low	Medium
Low. *t (df)*	2.74 (24)		
p (*d*)	.011 (.39)		
Medium. *t (df)*	4.59 (24)	4.39 (24)	
p (*d*)	.000 (.93)	.000 (.65)	
High. *t (df)*	6.55 (24)	6.89 (24)	2.85 (24)
p (*d*)	.000 (1.23)	.000 (1.03)	.009 (.43)
LF Group			
Low. *t (df)*	1.90 (11)		
p (*d*)	.084		
Medium. *t (df)*	3.73 (11)	4.19 (11)	
p (*d*)	.003 (1.44)	.002 (.68)	
High. *t (df)*	6.15 (11)	10.56 (11)	3.15 (11)
p (*d*)	.000 (1.92)	.000 (1.03)	.009 (.96)
HF Group			
Low. *t (df)*	2.14 (12)		
p (*d*)	.053		
Medium. *t (df)*	3.26 (12)	2.41 (12)	
p (*d*)	.007 (1.28)	.033 (.74)	
High. *t (df)*	5.74 (12)	4.11 (12)	.93 (12)
p (*d*)	.000 (1.56)	.001 (1.08)	.369

Note. Bold type indicates significance at $p < .05$.

Table 10

T score, p value and Cohen's d value results for dependent measures t-test on Energy Intake *at Test Time #1 during 0-180 minutes for both groups combined, followed by the LF and HF groups.*

	Vehicle	Low	Medium
Low. *t (df)*	1.95 (24)		
p (*d*)	.063		
Medium. *t (df)*	3.38 (24)	2.25 (24)	
p (*d*)	.002 (.56)	.034 (.33)	
High. *t (df)*	6.89 (24)	5.58 (24)	4.51 (24)
p (*d*)	.000 (1.12)	.000 (.93)	.000 (.66)
LF Group			
Low. *t (df)*	1.22 (11)		
p (*d*)	.249		
Medium. *t (df)*	2.63 (11)	2.09 (11)	
p (*d*)	.023 (.99)	.061	
High. *t (df)*	7.30 (11)	6.14 (11)	4.25 (11)
p (*d*)	.000 (1.96)	.000 (2.06)	.001 (1.32)
HF Group			
Low. *t (df)*	1.64 (12)		
p (*d*)	.127		
Medium. *t (df)*	2.59 (12)	1.069 (12)	
p (*d*)	.024 (.78)	.306	
High. *t (df)*	4.76 (12)	3.86 (12)	2.48 (12)
p (*d*)	.000 (1.58)	.002 (1.46)	.029 (.88)

Note. Bold type indicates significance at $p < .05$.

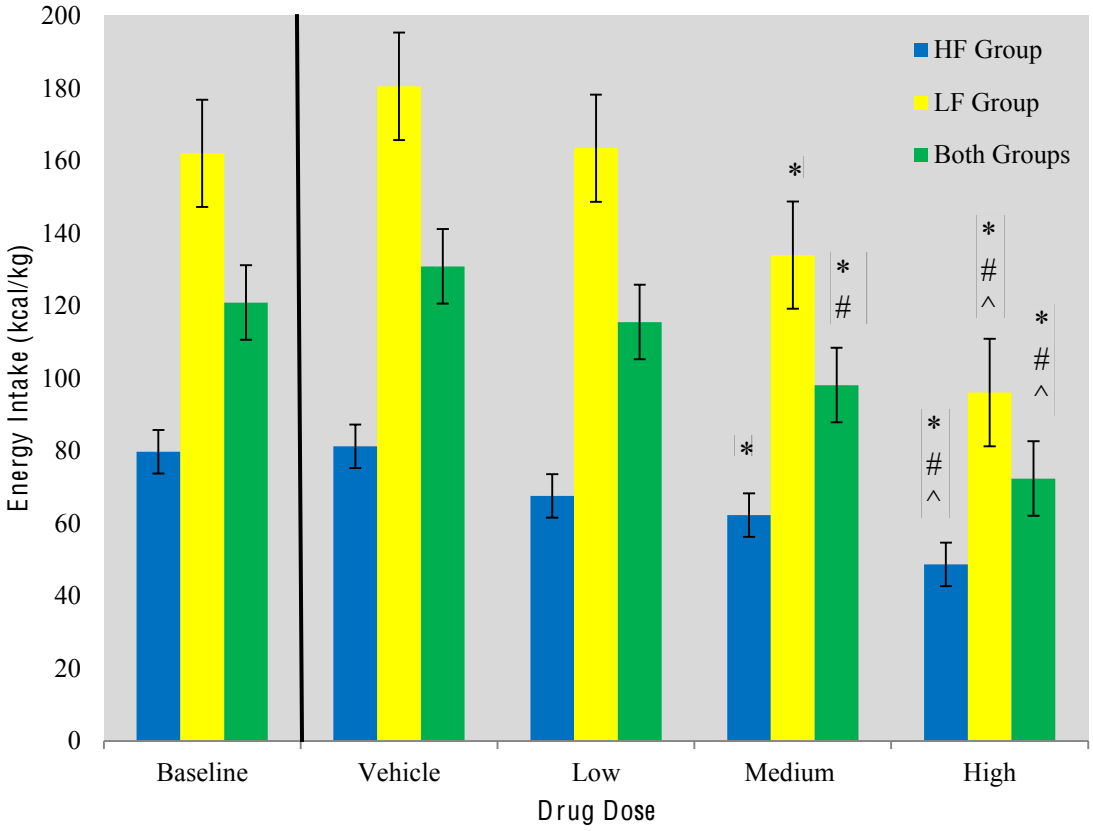

Figure 2. Energy Intake for the HF, LF, and both groups combined across all drug doses during the 0-180 minute time period at Test Time #1. Baseline was not included in the drug dose comparison analysis. The LF group had a significantly higher energy intake compared to the HF group. * indicates significantly decreased intake compared to the vehicle. # indicates significantly decreased compared to the low dose. ^ indicates significantly decreased compared to medium dose, $p < .05$. Error bars represent +/- 1 SE.

Table 11

Mean (SD) of Fat Preference *for both diet groups and all drug doses for interval test periods at Test Time #1.*

Diet Group	Baseline	Vehicle (0)	Low (.01)	Medium (.05)	High (.1)
0-30 minutes					
LF Group	.36 (.06)	.36 (.06)	.28 (.07)	.21 (.09)	.26 (.12)
HF Group	.38 (.05)	.33 (.11)	.22 (.12)	.21 (.12)	.12 (.10)
Total	.37 (.06)	.34 (.09)	.25 (.10)	.21 (.10)	.19 (.13)
30-60 minutes					
LF Group	.38 (.05)	.33 (.16)	.36 (.10)	.25 (.19)	.03 (.06)
HF Group	.33 (.16)	.26 (.20)	.21 (.21)	.22 (.21)	.22 (.20)
Total	.35 (.12)	.30 (.18)	.28 (.18)	.24 (.19)	.13 (.18)
60-120 minutes					
LF Group	.37 (.12)	.31 (.16)	.39 (.06)	.33 (.16)	.26 (.18)
HF Group	.27 (.17)	.31 (.15)	.28 (.18)	.23 (.20)	.26 (.18)
Total	.32 (.16)	.31 (.15)	.33 (.14)	.28 (.18)	.19 (.18)
120-180 minutes					
LF Group	.34 (.06)	.33 (.12)	.36 (.06)	.35 (.11)	.32 (.13)
HF Group	.32 (.15)	.35 (.09)	.25 (.18)	.33 (.14)	.24 (.16)
Total	.34 (.11)	.34 (.11)	.30 (.14)	.34 (.13)	.28 (.15)

Table 12

Mean (SD) of Fat Preference *for both diet groups and all drug doses for all cumulative test periods at Test Time #1.*

Diet Group	Baseline	Vehicle (0)	Low (.01)	Medium (.05)	High (.1)
0-30 minutes					
LF Group	.36 (.06)	.36 (.06)	.28 (.07)	.21 (.09)	.26 (.12)
HF Group	.38 (.05)	.33 (.11)	.22 (.12)	.21 (.12)	.12 (.10)
Total	.37 (.06)	.34 (.09)	.25 (.10)	.21 (.10)	.19 (.13)
0-60 minutes					
LF Group	.36 (.05)	.36 (.058)	.30 (.06)	.22 (.08)	.21 (.10)
HF Group	.38 (.04)	.34 (.09)	.25 (.10)	.21 (.07)	.14 (.08)
Total	.37 (.04)	.35 (.07)	.28 (.09)	.22 (.07)	.17 (.09)
0-120 minutes					
LF Group	.38 (.03)	.38 (.05)	.39 (.04)	.39 (.03)	.26 (.09)
HF Group	.37 (.05)	.33 (.09)	.28 (.06)	.22 (.06)	.18 (.08)
Total	.38 (.04)	.36 (.07)	.34 (.07)	.30 (.10)	.22 (.09)
0-180 minutes					
LF Group	.36 (.03)	.38 (.04)	.38 (.02)	.38 (.03)	.32 (.06)
HF Group	.36 (.05)	.34 (.08)	.29 (.06)	.27 (.08)	.21 (.07)
Total	.37 (.04)	.36 (.07)	.34 (.06)	.32 (.08)	.26 (.08)

Table 13

Independent measures t-test between the HF and LF groups at all time periods for Fat Preference *at Baseline #1.*

Time Interval	*df*	*t*	*p*	*d*
0-30	23	-.80	.432	.36
30-60	23	1.10	.291	.42
60-120	23	1.64	.115	.68
120-180	23	.28	.781	.09
Time Cumulative				
0-30	23	-.80	.432	.36
0-60	23	-.85	.403	.44
0-120	23	.51	.617	.24
0-180	23	-.07	.943	0

Table 14

Dependent measures t-tests on the amount of Fat Preference *for the HF and LF groups combined at Baseline #1 compared to vehicle at all time periods.*

Time Interval	*df*	*t*	*p*	*d*
0-30	24	1.77	.089	.39
30-60	24	1.04	.307	.33
60-120	24	.30	.767	.06
120-180	24	-.19	.852	0
Time Cumulative				
0-30	24	1.77	.089	.39
0-60	24	1.35	.189	.35
0-120	**24**	**2.06**	**.050**	**.35**
0-180	24	1.12	.276	.18

Note. **Bold type** indicates fat preference was significantly higher with baseline compared to vehicle, $p < .05$.

Table 15

T score, p value and Cohen's d value results for dependent measures t-test on Fat Preference *at Test Time #1 during 0-60, 0-120, and 0-180 minutes for both groups.*

0-60 Minutes	Vehicle	Low	Medium
Low. *t (df)*	3.22 (24)		
p (*d*)	.004 (.87)		
Medium. *t (df)*	7.99 (24)	2.89 (24)	
p (*d*)	.000 (1.86)	.008 (.74)	
High. *t (df)*	8.40 (24)	4.51 (24)	2.49 (24)
p (*d*)	.000 (2.23)	.000 (1.22)	.020 (.62)

0-120 Minutes	Baseline	Vehicle	Low	Medium
Vehicle. *t (df)*	2.22 (24)			
p (*d*)	.036 (.35)			
Low. *t (df)*	5.90 (24)	2.63 (24)		
p (*d*)	.000 (1.18)	.015 (.61)		
Medium. *t (df)*	7.81 (24)	5.99 (24)	3.29 (24)	
p (*d*)	.000 (2.11)	.000 (1.43)	.003 (.92)	
High. *t (df)*	11.12 (24)	8.90 (24)	7.46 (24)	3.60 (24)
p (*d*)	.000 (2.85)	.000 (2.13)	.000 (1.70)	.001 (.80)

0-180 Minutes	Vehicle	Low	Medium
Low. *t (df)*	1.75 (24)		
p (*d*)	.093		
Medium. *t (df)*	2.38 (24)	.87 (24)	
p (*d*)	.026 (.53)	.395	
High. *t (df)*	6.69 (24)	4.94 (24)	4.83 (24)
p (*d*)	.026 (1.33)	.000 (1.13)	.000 (.75)

Note. Bold type indicates significance at $p < .05$.

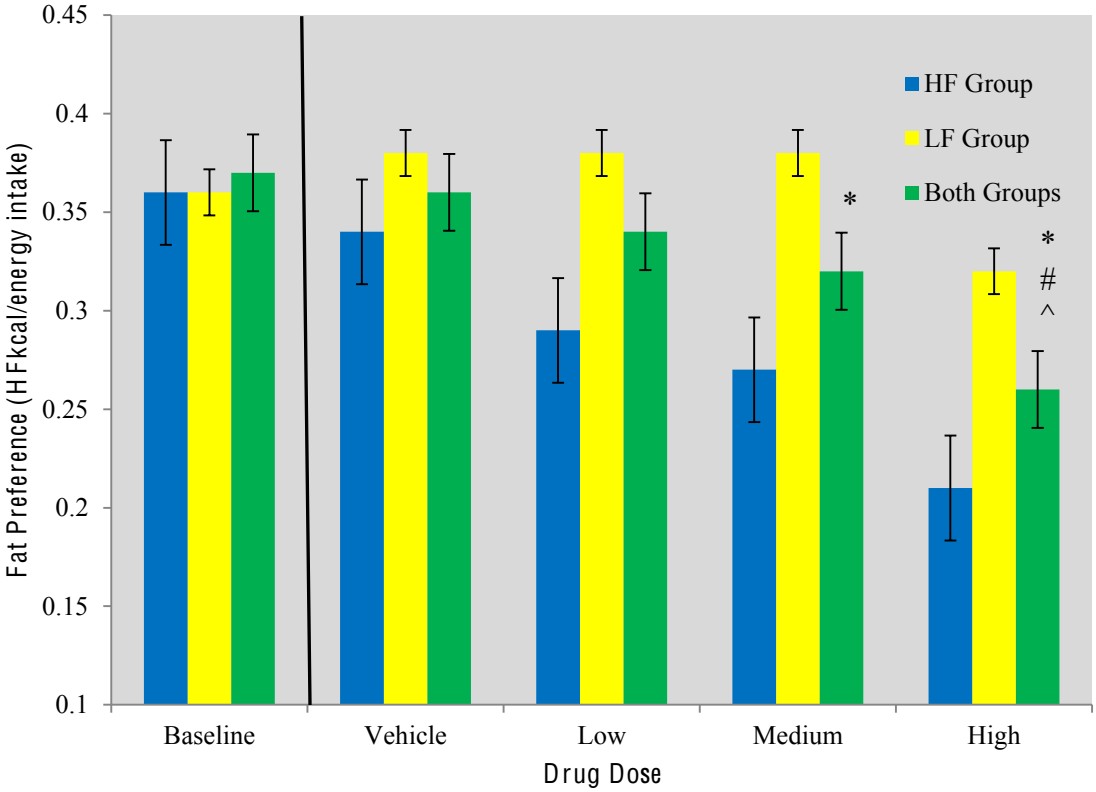

Figure 3. Fat preference for the HF and LF and both groups combined across all drug doses during the 0-180 minute time period at Test Time #1. Baseline was not included in the drug dose comparison analysis. The LF group significantly preferred high fat food more than the HF group. * indicates significantly less fat preference than the vehicle. # indicates significantly less than the low dose. ^ indicates significantly less than medium dose, $p < .05$. Error bars represent +/- 1 SE.

Table 16

Mean (SD) of Energy Intake *for both diet groups and all drug doses for all interval test periods at Test Time #2.*

Diet Group	Baseline	Vehicle (0)	Low (.01)	Medium (.05)	High (.1)
0-30 minutes					
LF Group	63.3 (27.3)	73.3 (23.9)	58.8 (16.5)	38.4 (12.8)	32.9 (17.9)
HF Group	67.2 (20.6)	52.9 (19.7)	47.2 (12.0)	36.6 (14.4)	34.4 (12.5)
Total	65.3 (23.6)	62.7 (23.7)	52.8 (15.2)	37.5 (13.4)	33.7 (15.1)
30-60 minutes					
LF Group	34.6 (15.5)	28.4 (16.8)	21.4 (14.0)	21.3 (14.7)	11.5 (8.0)
HF Group	22.6 (19.3)	27.4 (14.2)	13.6 (13.7)	13.0 (14.5)	2.1 (4.0)
Total	28.4 (18.2)	27.9 (15.2)	17.3 (14.2)	17.0 (14.9)	6.6 (7.7)
60-120 minutes					
LF Group	19.4 (10.7)	20.9 (12.2)	12.6 (12.4)	13.8 (11.5)	12.3 (13.9)
HF Group	11.7 (12.9)	13.8 (12.1)	13.5 (14.2)	14.2 (12.7)	17.1 (14.6)
Total	15.4 (12.3)	17.2 (12.4)	13.1 (13.1)	14.0 (11.9)	14.8 (14.2)
120-180 minutes					
LF Group	26.7 (13.5)	29.5 (19.6)	39.6 (15.6)	34.8 (18.4)	20.1 (12.6)
HF Group	21.9 (19.9)	26.2 (18.0)	27.3 (10.6)	35.9 (14.2)	22.5 (14.3)
Total	24.2 (16.9)	27.8 (18.5)	33.2 (14.4)	35.4 (16.0)	21.3 (13.3)

Table 17

Mean (SD) of Energy Intake *for both diet groups and all drug doses for all cumulative test periods at Test Time #2.*

Diet Group	Baseline	Vehicle (0)	Low (.01)	Medium (.05)	High (.1)
		0-30 minutes			
LF Group	63.3 (27.3)	73.3 (23.9)	58.8 (16.5)	38.4 (12.8)	32.9 (17.9)
HF Group	67.2 (20.6)	52.9 (19.7)	47..2 (12.0)	36.6 (14.4)	34.4 (12.5)
Total	65.3 (23.6)	62.7 (23.7)	52.8 (15.2)	37.5 (13.4)	33.7 (15.1)
		0-60 minutes			
LF Group	97.9 (28.9)	101.6 (18.9)	80.2 (24.7)	59.7 (21.3)	44.5 (18.0)
HF Group	89.8 (29.9)	80.3 (25.1)	60.8 (14.8)	49.5 (10.5)	36.5 (11.9)
Total	93.7 (29.1)	90.5 (24.5)	70.1 (22.0)	54.4 (17.0)	40.3 (15.4)
		0-120 minutes			
LF Group	117.3 (27.1)	122.5 (22.8)	92.8 (30.7)	73.5 (24.9)	56.6 (23.1)
HF Group	101.6 (25.4)	94.1 (27.3)	74.3 (25.6)	63.8 (13.2)	53.6 (14.8)
Total	109.1 (26.9)	107.7 (28.7)	83.2 (29.1)	68.5 (19.9)	55.1 (18.9)
		0-180 minutes			
LF Group	144.0 (29.6)	152.0 (26.6)	132.4 (38.6)	108.4 (26.3)	76.7 (27.7)
HF Group	123.5 (31.6)	120.2 (35.4)	101.6 (28.4)	99.6 (20.2)	76.1 (18.0)
Total	133.3 (31.8)	135.5 (34.8)	116.4 (36.5)	103.8 (23.2)	76.4 (22.7)

Table 18

Independent measures t-tests on Energy Intake *between the HF and LF groups at all time periods during Baseline #2.*

Time Interval	*df*	*t*	*p*	*d*
0-30	23	-.41	.688	.16
30-60	23	1.68	.103	.69
60-120	23	1.62	.120	.65
120-180	23	.70	.489	.28
Time Cumulative				
0-30	23	-.41	.688	.16
0-60	23	.68	.501	.28
0-120	23	1.50	.147	1.22
0-180	23	1.67	.108	.67

Table 19

Dependent measures t-tests on Energy Intake *for the HF and LF groups combined at Baseline #2 compared to vehicle at all time periods.*

Time Interval	*df*	*t*	*p*	*d*
0-30	24	.57	.572	.11
30-60	24	.11	.917	.03
60-120	24	-.56	.580	.15
120-180	24	-.87	.391	.20
Time Cumulative				
0-30	24	.57	.572	.11
0-60	24	.75	.458	.12
0-120	24	.36	.722	.05
0-180	24	-.56	.578	.07

Table 20

T score, p value and Cohen's d value results for dependent measures t-test on Energy Intake *at Test Time #2 during 0-180 minutes for both groups followed by LF and then HF group.*

	Vehicle	Low	Medium
Low. *t (df)*	3.78 (24)		
p (*d*)	.001 (.54)		
Medium. *t (df)*	5.66 (24)	2.43 (24)	
p (*d*)	.000 (1.07)	.023 (.41)	
High. *t (df)*	8.56 (24)	6.30 (24)	5.64 (24)
p (*d*)	.000 (2.01)	.000 (1.32)	.000 (1.19)
LF Group			
Low. *t (df)*	2.18 (11)		
p (*d*)	.052		
Medium. *t (df)*	5.68 (11)	2.96 (11)	
p (*d*)	.000 (1.65)	.013 (.73)	
High. *t (df)*	8.42 (11)	6.48 (11)	4.21 (11)
p (*d*)	.000 (2.77)	.000 (1.66)	.001 (1.17)
HF Group			
Low. *t (df)*	3.43 (12)		
p (*d*)	.005 (.58)		
Medium. *t (df)*	2.94 (12)	.38 (12)	
p (*d*)	.012 (.72)	.712	
High. *t (df)*	5.03 (12)	3.40 (12)	3.69 (12)
p (*d*)	.000 (1.57)	.005 (1.07)	.003 (1.23)

Note. **Bold type** indicates significance at $p < .05$.

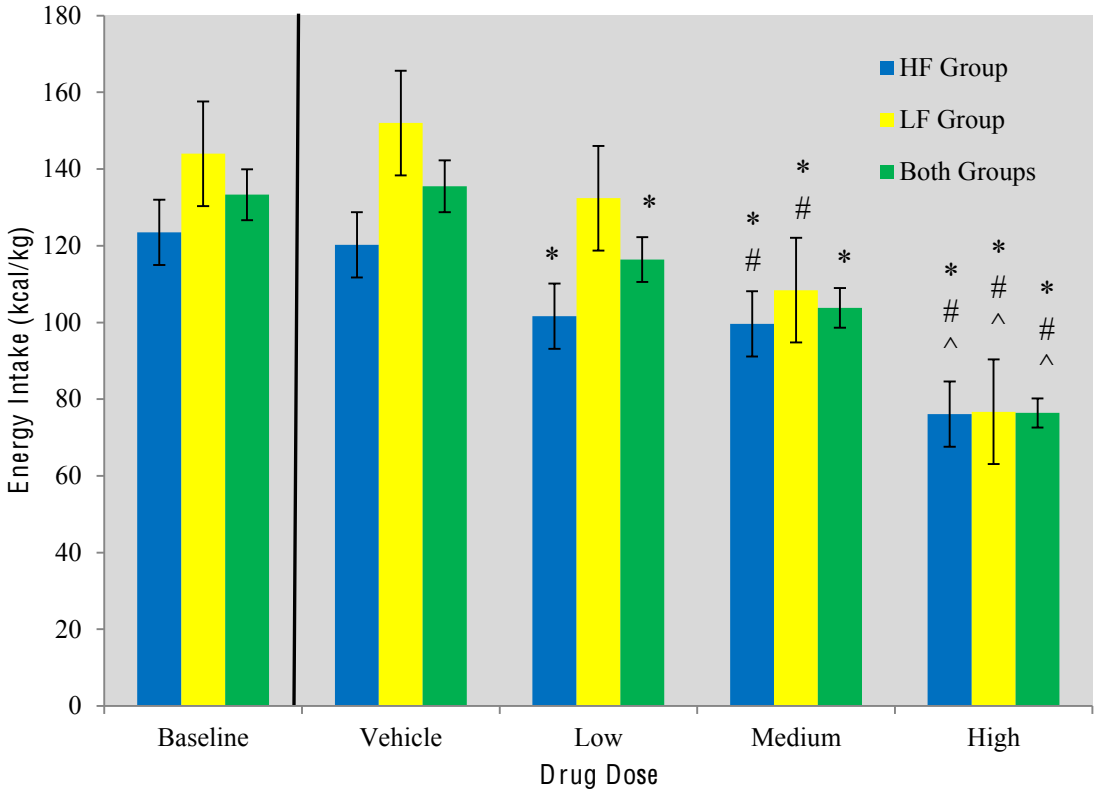

Figure 4. Energy Intake for the HF, LF, and both groups combined across all drug doses during the 0-180 minute time period at Test Time #2. Baseline was not included in the drug dose comparison analysis. There was no difference between the LF and HF groups. * indicates significantly less energy intake than the vehicle. # indicates significantly less than the low dose. ^ indicates significantly less than the medium dose, $p < .05$. Error bars represent +/- 1 SE.

Table 21

Mean (SD) of Fat Preference *for both diet groups and all drug doses for interval test periods at Test Time #2.*

Diet Group	Baseline	Vehicle (0)	Low (.01)	Medium (.05)	High (.1)
0-30 minutes					
LF Group	.45 (.05)	.42 (.06)	.31 (.07)	.20 (.07)	.18 (.11)
HF Group	.44 (.04)	.43 (.06)	.32 (.11)	.25 (.16)	.21 (.13)
Total	.44 (.04)	.42 (.06)	.32 (.09)	.22 (.13)	.19 (.12)
30-60 minutes					
LF Group	.46 (.04)	.43 (.14)	.35 (.17)	.38 (.14)	.18 (.18)
HF Group	.31 (.20)	.44 (.05)	.29 (.24)	.23 (.23)	.09 (.18)
Total	.38 (.16)	.43 (.10)	.32 (.21)	.30 (.20)	.13 (.18)
60-120 minutes					
LF Group	.42 (.08)	.31 (.15)	.23 (.23)	.32 (.21)	.21 (.22)
HF Group	.20 (.23)	.26 (.23)	.24 (.23)	.25 (.22)	.24 (.20)
Total	.31 (.20)	.28 (.19)	.23 (.22)	.29 (.21)	.23 (.21)
120-180 minutes					
LF Group	.33 (.17)	.42 (.07)	.39 (.10)	.33 (.16)	.25 (.19)
HF Group	.33 (.19)	.31 (.19)	.36 (.14)	.39 (.08)	.26 (.17)
Total	.33 (.18)	.37 (.15)	.38 (.12)	.36 (.13)	.26 (.18)

Table 22

Mean (SD) of Fat Preference *for both diet groups and all drug doses for all cumulative test periods at Test Time #2.*

Diet Group	Baseline	Vehicle (0)	Low (.01)	Medium (.05)	High (.1)
0-30 minutes					
LF Group	.45 (.05)	.42 (.06)	.31 (.07)	.20 (.07)	.18 (.11)
HF Group	.44 (.04)	.43 (.06)	.32 (.11)	.25 (.16)	.21 (.13)
Total	.44 (.04)	.42 (.06)	.32 (.09)	.22 (.13)	.19 (.12)
0-60 minutes					
LF Group	.46 (.04)	.43 (.05)	.34 (.06)	.25 (.08)	.21 (.08)
HF Group	.43 (.05)	.43 (.05)	.34 (.11)	.31 (.07)	.20 (.12)
Total	.44 (.05)	.43 (.05)	.34 (.09)	.28 (.08)	.21 (.10)
0-120 minutes					
LF Group	.45 (.05)	.42 (.05)	.35 (.06)	.28 (.07)	.22 (.08)
HF Group	.42 (.04)	.42 (.06)	.35 (.11)	.32 (.07)	.24 (.13)
Total	.43 (.05)	.42 (.05)	.35 (.09)	.30 (.07)	.23 (.10)
0-180 minutes					
LF Group	.43 (.04)	.42 (.04)	.36 (.04)	.32 (.07)	.25 (.06)
HF Group	.43 (.04)	.42 (.05)	.36 (.10)	.35 (.06)	.26 (.11)
Total	.43 (.04)	.42 (.04)	.36 (.07)	.33 (.06)	.26 (.09)

Table 23

Independent measures t-test between the HF and LF groups at all time periods on Fat Preference *during Baseline #2*.

Time Interval	*df*	*t*	*p*	*d*
0-30	23	.86	.401	.02
30-60	**13.0**	**2.59**	**.023**	**1.04**
60-120	**15.2**	**3.31**	**.005**	**1.28**
120-180	23	-.04	.968	0
Time Cumulative				
0-30	23	.86	.401	.02
0-60	23	1.50	.148	.66
0-120	23	1.50	.146	.66
0-180	23	.46	.653	0

Note. **Bold type** indicates the HF group significantly preferred the high fat food less than the HF group, $p < .05$.

Table 24

Dependent measures t-tests on Fat Preference *for the HF and LF groups combined at Baseline #2 compared to vehicle at all time periods.*

Time Interval	*df*	*t*	*p*	*d*
0-30	**24**	**2.44**	**.022**	**.42**
30-60	24	-1.34	.194	.38
60-120	24	.44	.667	.15
120-180	24	-.73	.475	.24
Time Cumulative				
0-30	**24**	**2.44**	**.022**	**.42**
0-60	24	1.29	.211	.20
0-120	24	1.70	.102	.29
0-180	**24**	**2.10**	**.046**	**.30**

Note. **Bold type** indicates fat preference was significantly higher at baseline compared to vehicle, $p < .05$.

Table 25

T score, p value and Cohen's d value results for dependent measures t-test on Fat Preference *at Test Time #2 during 0-30 minutes.*

	Baseline	Vehicle	Low	Medium
Vehicle. *t*	2.44			
p (*d*)	.022 (.39)			
Low. *t*	6.18	5.02		
p (*d*)	.000 (1.72)	.000 (1.31)		
Medium. *t*	9.13	8.34	3.50	
p (*d*)	.000 (2.29)	.000 (1.98)	.002 (.89)	
High. *t*	10.99	9.71	5.52	.94
p (*d*)	.000 (2.80)	.000 (2.42)	.000 (1.23)	.357

Note. Bold type indicates significance at $p < .05$. Degrees of freedom = 24 for all t-tests.

Table 26

T score, p value and Cohen's d value results for dependent measures t-test on Fat Preference *at Test Time #2 during 0-60, 0-120, and 0-180 minutes for both groups.*

0-60 Minutes	Vehicle	Low	Medium
Low. *t (df)*	4.94 (24)		
p (*d*)	.000 (1.24)		
Medium. *t (df)*	8.66 (24)	2.63 (24)	
p (*d*)	.000 (2.25)	.015 (.71)	
High. *t (df)*	11.34 (24)	6.19 (24)	3.05 (24)
p (*d*)	.000 (2.78)	.000 (1.37)	.006 (.81)

0-120 Minutes	Vehicle	Low	Medium
Low. *t (df)*	3.79 (24)		
p (*d*)	.001 (.96)		
Medium. *t (df)*	7.64 (24)	2.31 (24)	
p (*d*)	.000 (1.97)	.030 (.62)	
High. *t (df)*	9.43 (24)	5.12 (24)	2.65 (24)
p (*d*)	.000 (2.40)	.000 (1.16)	.014 (.81)

0-180 Minutes	Baseline	Vehicle	Low	Medium
Vehicle. *t (df)*	2.10 (24)			
p (*d*)	.046 (.25)			
Low. *t (df)*	5.10 (24)	3.36 (24)		
p (*d*)	.000 (1.23)	.003 (1.05)		
Medium. *t (df)*	6.83 (24)	6.06 (24)	2.01 (24)	
p (*d*)	.000 (1.96)	.000 (1.77)	.056	
High. *t (df)*	9.13 (24)	8.37 (24)	6.93 (24)	3.82 (24)
p (*d*)	.000 (2.44)	.000 (2.30)	.000 (1.24)	.001 (.92)

Note. Bold type indicates significance, $p < .05$.

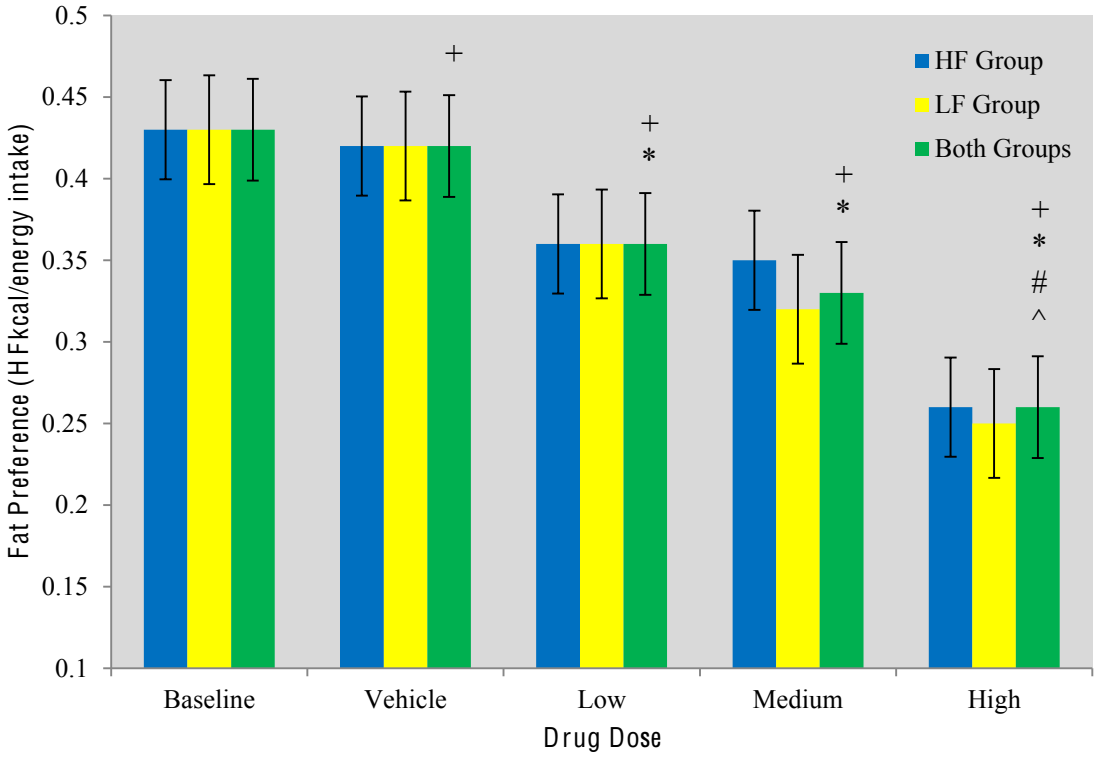

Figure 5. Fat preference for the HF and LF and both groups combined across all drug doses during the 0-180 minute time period at Test Time #2. There was no difference in fat preference between the HF and LF group. + indicates significantly less fat preference than baseline. * indicates significantly less than the vehicle. # indicates significantly less than the low dose. ^ indicates significantly less than the medium dose, $p < .05$. Error bars represent +/- 1 SE.

Table 27

Results of 2 X 2 Mixed ANOVA for Fat Preference *with vehicle and low dose at all cumulative time periods. Diet group was HF versus LF Group (between factor), Test Time was Test Time #1 versus Test Time #2 (within factor), and diet group versus test time was the interaction.*

Vehicle		Diet Group		Low Dose		Diet Group	
	$F(1, 23)$	p	η^2		$F(1, 23)$	p	η^2
0-30	.07	.791	.00	0-30	.68	.418	.03
0-60	.29	.595	.01	0-60	1.59	.211	.07
0-120	.29	.631	.01	0-120	.76	.391	.03
0-180	.41	.528	.02	0-180	1.48	.237	.06
		Test Time				Test Time	
	$F(1, 23)$	p	η^2		$F(1, 23)$	p	η^2
0-30	**19.74**	**.000**	**.46**	0-30	**6.34**	**.019**	**.22**
0-60	**25.78**	**.000**	**.53**	0-60	**6.12**	**.021**	**.21**
0-120	**26.67**	**.000**	**.54**	0-120	**4.82**	**.038**	**.17**
0-180	**32.73**	**.000**	**.59**	0-180	**8.43**	**.008**	**.27**
		Interaction				Interaction	
	$F(1, 23)$	p	η^2		$F(1, 23)$	p	η^2
0-30	1.22	.281	.05	0-30	1.49	.235	.06
0-60	.30	.590	.01	0-60	1.75	.199	.07
0-120	.68	.420	.03	0-120	1.55	.226	.06
0-180	.64	.433	.03	0-180	1.74	.201	.07

Note. **Bold type** indicates significance at $p < .05$.

Table 28

Results of 2 X 2 Mixed ANOVA for Fat Preference *with medium and high dose at all cumulative time periods. Diet group was HF versus LF Group (between factor), Test Time was Test Time #1 versus Test Time #2 (within factor), and diet group versus test time was the interaction.*

Medium Dose	Diet Group			High Dose	Diet Group		
	$F(1, 23)$	p	η^2		$F(1, 23)$	p	η^2
0-30	.64	.431	.03	0-30	2.17	.154	.09
0-60	1.24	.277	.05	0-60	1.47	.239	.06
0-120	.14	.711	.01	0-120	.00	.988	.00
0-180	.06	.807	.00	0-180	.09	.768	.00
	Test Time				Test Time		
	$F(1, 23)$	p	η^2		$F(1, 23)$	p	η^2
0-30	.18	.679	.01	0-30	.00	.963	.00
0-60	**9.18**	**.006**	**.29**	0-60	2.66	.117	.10
0-120	**6.39**	**.019**	**.22**	0-120	3.56	.072	.13
0-180	**9.73**	**.005**	**.30**	0-180	2.33	.141	.09
	Interaction				Interaction		
	$F(1, 23)$	p	η^2		$F(1, 23)$	p	η^2
0-30	.56	.462	.02	**0-30**	**8.16**	**.009**	**.26**
0-60	2.61	.120	.10	0-60	2.18	.153	.09
0-120	**5.55**	**.027**	**.19**	0-120	.77	.390	.03
0-180	**6.99**	**.015**	**.23**	0-180	.99	.329	.04

Note. **Bold type** indicates significance at $p < .05$

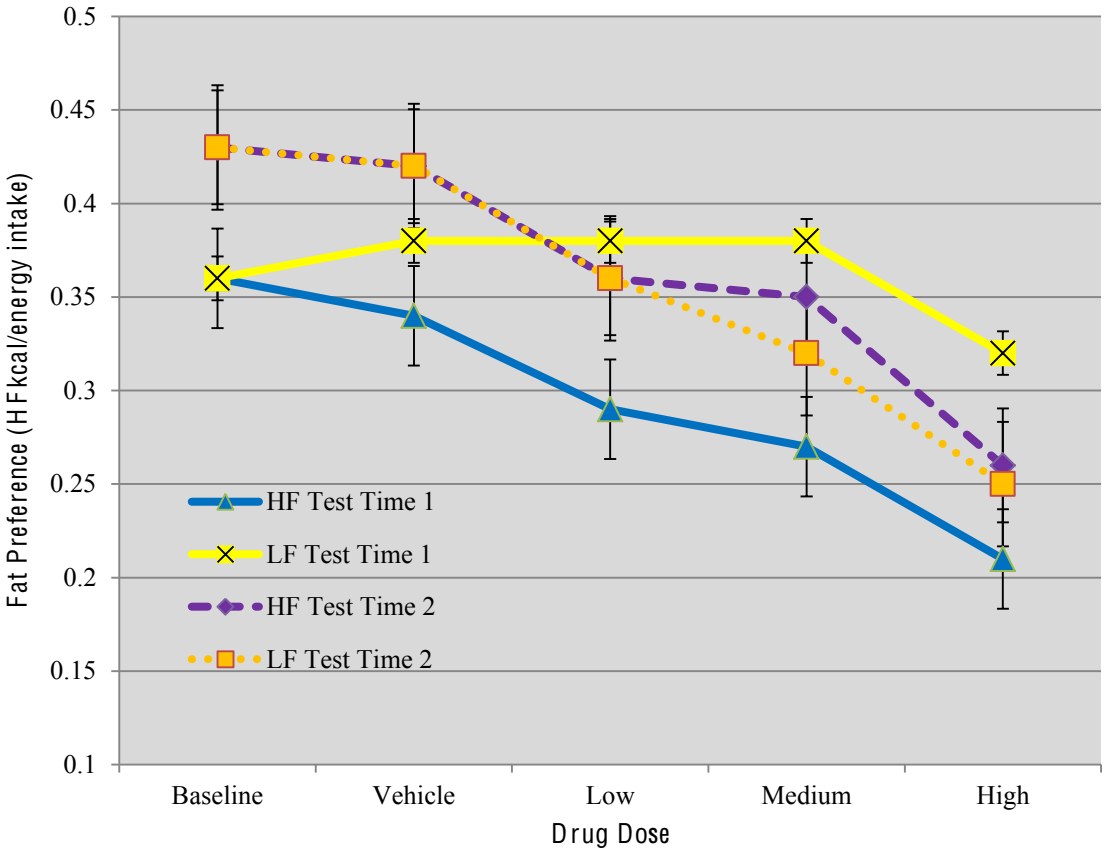

Figure 6. Fat Preference across all drug doses for the HF and LF group at Test Time #1 and #2. Error bars represent +/- 1 SE.

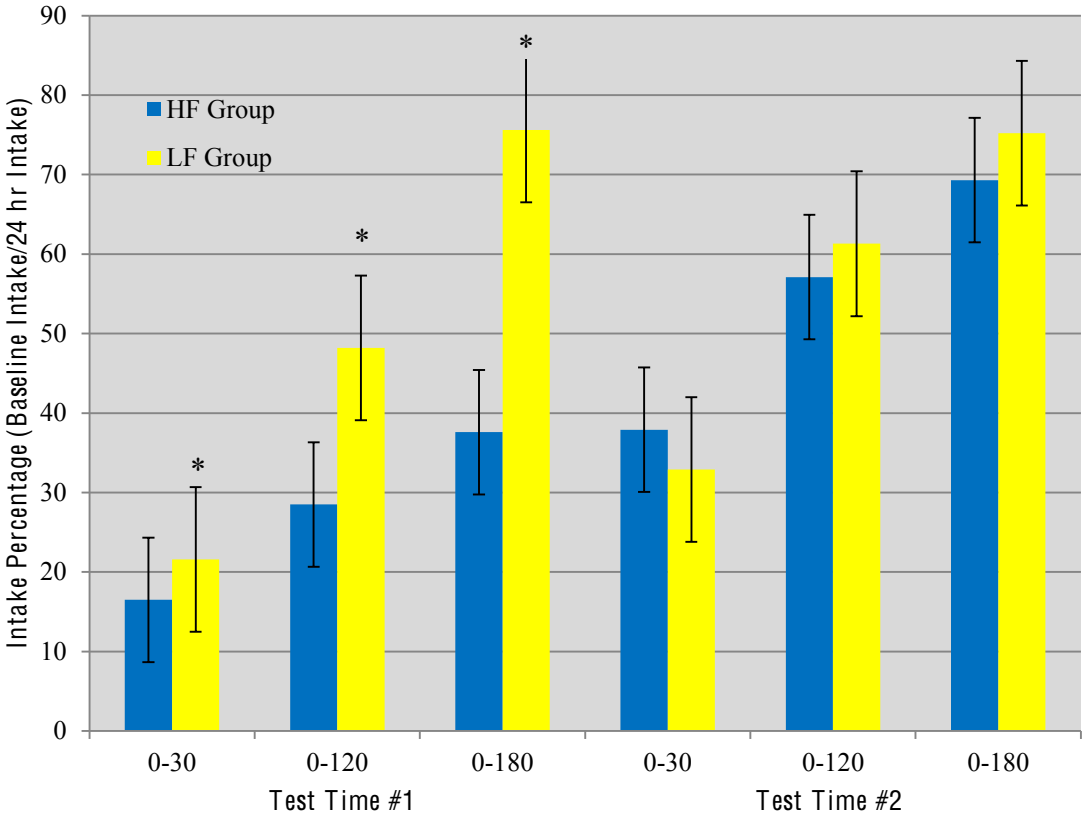

Figure 7. Intake Percentage of HF and LF groups during Test Time #1 and #2. * indicates significantly more than the HF group during that Test Time, $p < .05$. Error bars represent +/- 1 SE.

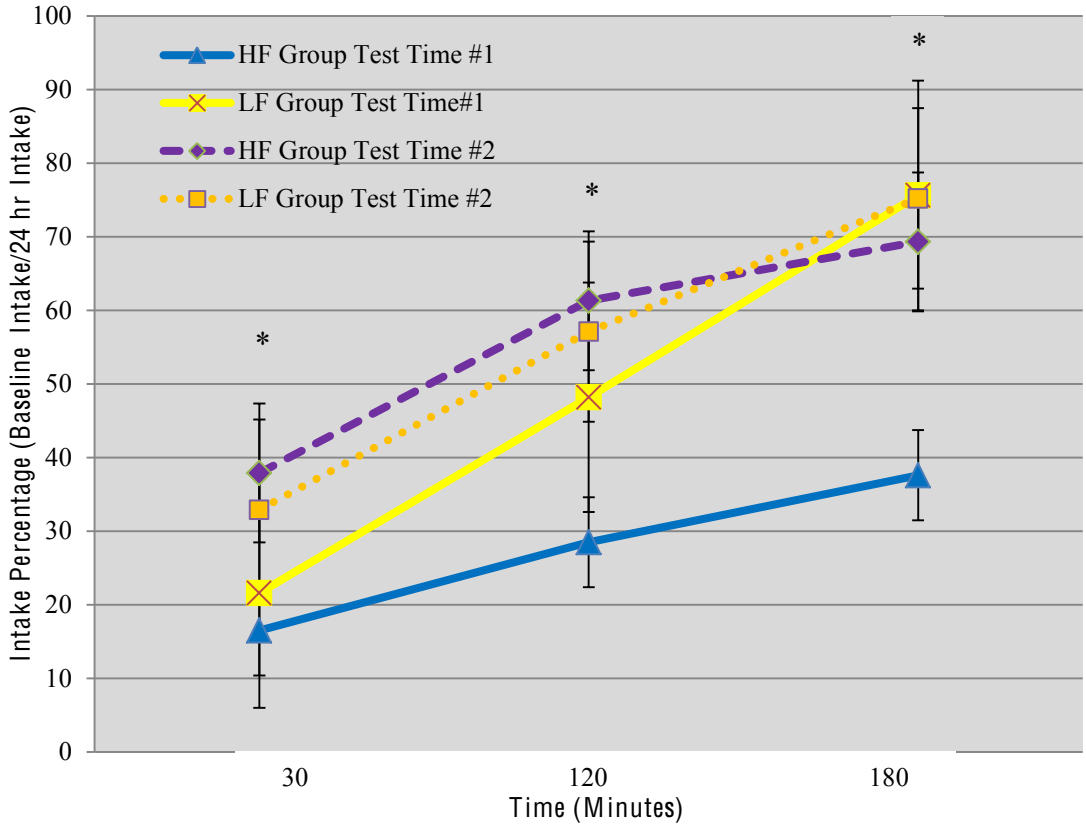

Figure 8. Cumulative Intake Percentage for the HF and LF group at Test Time #1 and #2. * indicates Intake Percentage for both groups combined was significantly higher at Test Time #2 compared to Test Time #1. Error bars represent +/- 1 SE.

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