Assessment of the Conditioned Taste Aversion Phenomenon Induced by Binge Eating

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Abstract:

A conditioned taste aversion created by a non-traditional paradigm using 24 hour access to a saccharin solution paired with binge eating was reported by Hertel and Eikelboom (2010). This experiment was replicated with the addition of a pre-exposure condition in order to determine if the results were truly a conditioned taste aversion. Adult male Sprague-Dawley rats were split into two groups restricted and *ab-libitum* food access for a total of 25 pre-exposure days. The rats were then split into two additional groups, creating a total of four groups of restricted-restricted, restricted-*ad-libitum*, *ad-libitum, ad-libitum,* and *ad-libitum*-restricted. The restricted groups were given access to an *ad-libitum* diet every 5th day, creating a bingeing cycle. During the acquisition phase, the overeating days were paired with a 0.1% saccharin solution. On the 24th day of conditioning all rats were given a two-bottle choice test. The restricted-restricted rats were the only group to demonstrate an aversion to the saccharin solution. It appears that a history of exposure to binge eating sensitizes the rats to the aversive components of the saccharin solution.

Introduction

In 1955, Garcia and his colleagues described the condition taste aversion phenomenon. In this study, a saccharin solution was paired with ionizing radiation. The saccharin solution is traditionally preferred over water by rats; however, when it became paired with the aversive aspects of ionizing radiation through classical conditioning, the saccharin solution was avoided, i.e., an aversion was formed. Conditioned taste aversion learning is most often used to assess the aversive aspects of drugs in the study of drug addiction (see Riley et al. 1976; Goudie et al., 1978). Although initially reported with a host of drugs, conditioned taste aversions can also be induced through methods other than drug administration. For example, conditioned taste aversions have been induced by wheel running (Lett et al., 2001) and forced swimming (Masaki & Nakajima, 2005).

In an extension of the types of stimuli able to induce taste aversions, Hertel and Eikelboom (2009) have recently reported that male rats who were previously food restricted and then allowed ad-libitum food access suppressed their feeding behavior the day after they were allowed free food access. This phenomenon has been called a post-gorging behavioral low (Lockard, 1967; Armstrong, 1980) and has been suggested to reflect an acquired aversion to the food as a consequence of the aversive effects produced by the increased food consumption occurring during the ad-libitum access period. The issue of satiety or nimiety (see Kulkosky, 1985) as an aversive event has a long and interesting history (Kulkosky and Gibbs, 1982; Perez and Scalafini, 1991; Scalafini and Ackroff, 2004). Specifically, Kulkosky and his colleagues have arued that nimiety occurs when an animal eats beyond satiation, and such an effect is sufficient to induce an aversion to a taste associated with this state (although see Holt et al. 1974).

To investigate the role of overeating in conditioned taste aversions, Hertel and Eikelboom (2010) used a restricted eating paradigm to pair binge eating with saccharin consumption. They found a significant conditioned taste aversion in the group that received restricted food access, where their binge eating was paired with saccharin consumption. If the suppression of food intake occurring following the free access is a function of an acquired aversion, then manipulations known to affect aversion conditioning should impact post-gorging suppression. Hertel and Eikelboom (2010) tested this hypothesis with a latent inihibition paradigm. Half of the rats received pre-exposure to a saccharin solution. The rats were then split into groups of restricted and *ad-libitum* food consumption. The binge eating was again paired with a saccharin solution. The restricted rats for whom the saccharin was novel experienced a decrease in saccharin consumption compared to the *ad-libitum* novel saccharin rats. The rats who had a familiarity with the saccharin solution did not experience an aversion to the saccharin solution.

Another manipulation known to affect taste aversion conditioning with more traditional aversive stimuli is a prior history with the aversion inducing agent (or manipulation). For example, exposure to a drug prior to aversion conditioning with the same drug weakens the acquisition of aversions (see Riley & Simpson 2001 for a review). Such effects are also reported when the preexposure and conditioning drugs are different (Switzman et al., 1981). If gorging-induced suppression is a form of a conditioned aversion, prior experience with *ad-libitum* feeding (following restricted access) should weaken the ability of gorging to induce an aversion to a solution associated with this state. This prediction was tested in the following experiment.

Specifically, animals with (and without) a history of binge eating were subjected to the restricted/free feeding procedure described above during which saccharin was made available.

Methods

Subjects

The subjects were 32 experimentally naïve male Sprague-Dawley rats, approximately 50 days of age and weighing between 200 and 225 g at the start of the experiment. Procedures recommended by the National Research Council (1996), the Committee on Guidelines for the Care and Use of Animals in Neuroscience and Behavioral Research (2003) and the Institutional Animal Care and Use Committee at American University were followed at all times. Animals were handled daily approximately two weeks prior to the initiation of the study to limit the effects of handling stress during conditioning and testing.

Apparatus

All subjects were individually housed in hanging wire-mesh cages on the front of which graduated Nalgene tubes could be placed for fluid presentation. Subjects were maintained on a 12:12 light-dark cycle (lights on at 0800h) and at an ambient temperature of 23 °C.

Procedure

Phase I: Preexposure. During this phase, rats were randomly assigned to two conditions. One group was given *ad libitum* access to Harlan Techlad 8640 lab chow (A). The other group was placed on a restricted diet (R). The amount of food consumed by the rats in Group A was determined, and this amount was reduced by 50% for the restricted

rats. Rats in the restricted group were given *ad libitum* access to food every 5th day for a period of 24 hours. This procedure (4 days restricted/one day *ad libitum*) was repeated for five complete cycles. On the day following the last cycle, the restricted rats returned to the restricted diet for 5 additional days.

Phase II: Conditioning. Conditioning began 5 days after the final pre-exposure trial. The rats in the *ad libitum* group (Group A) were randomly divided into two groups of eight subjects each. One group continued to receive *ad libitum* food access (Group AA); the other was placed under food restriction (Group AR). The rats in the restricted group (Group R) were also divided into two groups of eight subjects each. One group was given *ad libitum* access to food (Group RA); the other remained on restricted feeding (Group RR; see above). The first letter in each group designation refers to the condition during preexposure, i.e., *ad libitum* (A) or restricted feeding (R); the second letter refers to the condition during conditioning, i.e., *ad libitum* (A) or restricted feeding (R). On Days 1-8, the rats had access to their respective diets. On Days 9, 14 and 19 (the conditioning trials), all rats were given *ad libitum* access to food. During this access period, water was replaced with a 0.1% saccharin solution. On intervening days, the restricted rats (Groups AR and RR) returned to restricted food access, while the *ad libitum* groups (Groups AA and RA) had free food access. Following the final acquisition trial (Day 19), the rats returned to their respective diets. All rats were then given 3 days of *ad libitum* food access (Days 21-23).

Phase III: Two-bottle preference test. On Day 24, all rats were given 24-h access to both water and saccharin in a two-bottle preference test. Each rat was given access to

100 ml of water and 100 ml of a 0.1% saccharin solution counterbalanced to avoid a side preference.

Results

Preexposure

A repeated measures ANOVA (Day x Group) was run over the 25 day pre-exposure period to test the stability of food consumption of the *ad-libitum* rats. There was a significant interaction between day and group, $F(24, 720) = 141.828$, $p < .001$. The *ad-libitum* group displayed significantly different consumption during pre-exposure days. All days of pre-exposure were compared to the baseline consumption on Day 1. During Days 3 and 17, the average consumption was significantly higher than baseline, and during Days 6, 18, 20, 21, 22 and 23 food consumption was significantly lower than baseline, $p \leq .048$ (see Figure 1). A repeated measures ANOVA (Trial x Group) was run on the 5 trial days to examine the stability of the binge eating for the restricted rats. There was a significant interaction between trial and group, $F(4, 120) = 3.072$, $p < .05$. The 5 trial days were compared to the baseline binge eating trial, day 5. On day 3, the consumption was significantly higher than the baseline, $p < .05$ (see Figure 1)

Conditioning

Food consumption. A 3 (Trial) x 4 (Group) ANOVA on food consumption during conditioning revealed a significant interaction between trial and group, $F(6, 56) = 2.98$, $p < .05$. The restricted groups did not differ from each other in any trials. The *ad-libitum* groups differed during the first trial, with the RA group consuming significantly more food. During the first trial the restricted groups differed on their comparisons with the *ad-libitum* group. The RR group ate significantly more food than either *ad-libitum* groups,

whereas, the AR group only ate significantly more food than the AA group. During the trial 2 and 3, the restricted groups both ate significantly more food than the *ad-libitum* groups (see Figure 2).

Saccharin intake. Saccharin consumption was analyzed over the three acquisition days using a 3 (Trial) x 4 (Group) ANOVA. No significant differences were found in saccharin consumption among groups ($p = .288$) (see Figure 3).

Two-Bottle Test

A one way ANOVA on saccharin preference during the two bottle test administered on Day 23 revealed significant differences among groups, $F(1, 28) = 42.205$, $p < .001$. Specifically, Groups RR and AR displayed significantly higher saccharin preference than Groups AA and the RA.

A one way ANOVA on saccharin consumption revealed a significant effect of Group, $F(3,28) = 3.657$. $p < .05$. LSD post-hoc analysis revealed a significant difference in saccharin consumption. Group RR consumed significantly ($p < .05$) less saccharin than the other three groups (see Figures 4 and 5). Finally, a one way ANOVA performed on water consumption revealed significant differences among groups, $F(3,28) = 3.371$, $p < .05$. LSD post-hoc analysis revealed that Group RR consumed significantly ($p < .05$) more water than the three other groups (see Figure 5).

Discussion

The purpose of this study was to investigate Hertel and Eikelboom's (2010) conclusion that binge eating in male Sprague-Dawley rats induces a conditioned taste aversion. This study utilized a pre-exposure manipulation. A history of exposure to the binge eating paradigm was theorized to result in an attenuation of a conditioned taste

aversion. 16 male rats were placed in a restricted eating model (4 days of restricted eating, followed by 1 day *ad-libitum* access to food) and 16 male rats were allowed constant *ad-libitum* access to food. After 25 days of pre-exposure, the groups were split up into two more groups, for a total of four groups. The four groups were restricted-restricted, restricted-*ad-libitum*, *ad-libitum-ad-libitum,* and *ad-libitum*-restricted. Embedded in the conditioning phase of this experiment was a replication of Hertel and Eikelboom (2010) experiment. The groups were then presented with a two bottle choice test to evaluate if a conditioned taste aversion was present. Instead of replicating Hertel and Eikelboom's (2010) results; this study found that the rats who were restricted during pre-exposure displayed an aversion to the saccharin. The AR group, the replication group, did not display a significant aversion.

Why were these results different than that of Hertel and Eikelboom's (2010)? One option may be that this study did not induce binge eating. However, the restriction group displayed binge eating on the pre-exposure trial days (5, 10, 15, 20, 25) where they were presented with *ad-libitum* food access, when compared to the food consumption of *ad-libitum* group. During the conditioning trials, both restriction groups displayed binge eating compared to the *ad-libitum* groups.

Additionally, the percentage of saccharin consumed by the rats in this study is comparable to the estimated percentages in Hertel and Eikelboom's (2010) investigation. The estimated percentages in their study were as follows: the *ad-libitum* group had about a 97% saccharin preference, while the restricted group displayed about a 92% saccharin preference. The AA group in the present study demonstrated a 93.99% saccharin preference, the RA group displayed an 88.56% saccharin preference, the AR group

showed an 86.44% preference, and the RR group had a 70.95% preference. The difference between the percentages of the *ad-libitum* and restricted rats in Hertel and Eikelboom's (2010) study is only about 5%, while the difference between the same groups in the present study is actually higher at about 7%.

Another reason for the failed replication could be due to a differing in parameters. Both studies used a 12:12 hour light and dark cycle. The subjects were on the same restriction binge cycle, with 4 days of restriction followed by one day of *ad-libitum* food access to induce binge eating occurring after an initial restriction period. The rats had the same trial days (9, 14, and 19) during the conditioning phase. Both studies utilized a two-bottle test to evaluate the presence of a conditioned taste aversion.

While this study failed to replicate the conditioned taste aversion displayed by the restricted group in Hertel and Eikelboom's (2010) study, it did find a significant conditioned taste aversion in the RR group, who had a history of conditioned taste aversions. There are a number of explanations to account for this finding.

A history of exposure typically is known to attenuate a conditioned taste aversion. However, history may also result in sensitization to a stimulus. Sensitization is typically associated with increased motor activity when rats are pre-exposed to an amphetamine or to cocaine, (Vezina, 2007; Beyer & Steketee, 2002). In this experiment, a pre-exposure to binge eating may have sensitized the rats to the aversive aspects of binge eating. The trend of the AR groups' saccharin consumption revealed a lessening of consumption throughout the three trials. Additional pre-exposure and conditioning trials are necessary to investigate the possibility of sensitization.

Another possible explanation is that the bingeing behavior elicited by the RR group became pathological. Each binge eating trial may be mildly aversive, as shown by the general decrease of both the RR and AR groups' saccharin consumption. The RR group experienced 5 pre-exposure binge eating trials, which allowed the mildly aversive aspects of binge eating to accumulate. The schedule of restricting and bingeing may have created schedule induced polydipsia in the RR rats. Although most polydipsia research has found this phenomenon in rats who had a scheduled food bar press (see Falk, 1966), the binge eating schedule may have induced the same polydipsia in the RR rats. Additional trials would be helpful to see if this effect eventually occurred in the RA rats, or if the schedule induced polydispsia became more severe in the RR rats.

Additional research needs to be performed in order to investigate this phenomenon. The experiment only investigated the response of male Sprague-Dawley rats to the binge eating paradigm. Future research should examine the response of female rats, and male and female rats of other strains.

References

Armstrong, S., Coleman, G., & Singer, G. (1980). Food and water deprivation: changes in rat feeding, drinking, activity and body weight. *Neurosci. Biobehav. Rev. 4*(3), 377–402

Beyer, C. E. & Steketee, J. D. (2002). Cocaine Sensitization: Modulation by Dopamine D2 Receptors. *Cerebral Cortex, 12*(5), 526-535.

Falk, J. L. (1966). The motivational properties of schedule induced polydipsia. *J. exp. Anal. Behav.*, *9*(1), 19-25.

Garcia, J., Kimeldorf, D. J., & Koelling, R. A. (1955). Conditioned aversion to saccharin resulting from exposure to gamma radiation. *Science, 122*, 157–158.

Goudie, A. J., Dickins, D. W., & Thorton, E. W. (1978). Cocaine-induced conditioned taste aversions in rats. *Pharmacology Biochemistry and Behavior*, *8*(6), 757-761.

Hertel, A.; Parfeniuk, G.; Botzang, L.; Eikelboom, R. (2009). The effects of prior weight reduction on the running wheel-induced feeding suppression in rats. *Behav. Processes*, *82*(1), 56-61.

Hertel, A. & Eikelboom, R. (2010). Can overeating induce conditioned taste avoidance in previously food restricted rats? *Physiology & Behavior*, *99*(4), 482-486.

Holt, J. J., Antin, J., Gibbs, J., Young, R. C., & Smith, G. P. (1974). Cholecystokinin does not produce bait shyness in rats. *Physiol. Behav.*, *12*(3), 497-498.

Kulkosky, P. J. Conditioned food aversions and satiety signals. (1985). *Annals of the New York Academy of Sciences*, *443*, 330–347.

Kulkosky, P. J., D. J. Fanser, and J. Gibbs. (1981). Litocin suppresses food intake in rats. *Sot. Neurosci. Abstr. 7,* 852.

Lockard, R.B. (1967) Replacement behavior following deprivation of food, water, running, or light. *Psychol. Rep. 21*(3), 753–769.

Masaki, T. & Nakajima, S. (2005). Further evidence for conditioned taste aversion induced by forced swimming. *Physiology and Behavior, 84,* 9-15.

Perez, C., and A. Sclafani. (1991). Cholecystokinin conditions flavor preferences in rats. *Am. J. Physiol. 260,* 179-R185.

Riley, A. L., Jacobs, W. J., & LoLordo, V. M. (1976). Drug exposure and the acquisition and retention of a conditioned taste aversion. *Journal of Comparative and Physiological Psychology, 90*(8), 799–807

Riley, A. L. & Simpson, G. R. (2001) The attenuating effects of drug preexposure on taste aversion conditioning: generality, experimental parameters, underlying mechanisms and implications for drug use and abuse. In: Mowrer RR, Klein SB, editors. Contemporary learning theories. 2nd edition. Hillsdale, New Jersey: L. Erlbaum Assoc; 505–59.

Sclafani, A., Ackroff, K. (2004). The relationship between food reward and satiation revisited. *Physiol Behav, 82*(1)*,* 89–95.

Switzman, L., Fishman, B. & Amit, Z., (1981). Pre-exposure effects of morphine, diazepam and Δ^9. *Psychopharmacology, 74*(2), 149–157.

Vezina, P. (2007). Sensitization, drug addiction and psychopathology in animals and humans. *Progress in Neuro-Psychopharmacology and Biological Psychiatry, 31*(8), 1552-1555.

Figure 1

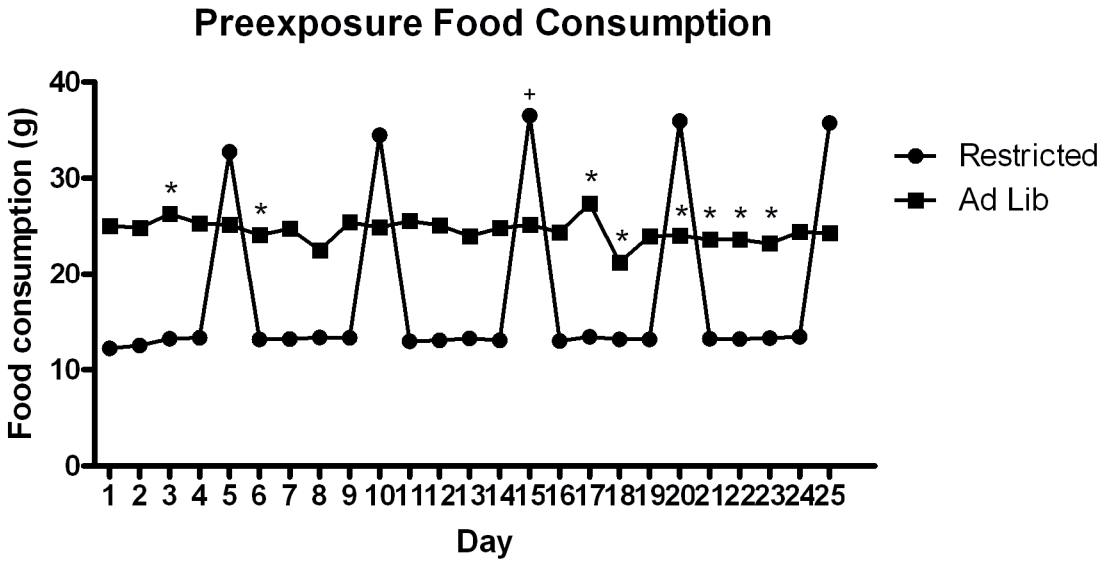

Preexposure Food Consumption
Food consumption (g)
0
10
20
30
40
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25
Day
Restricted
Ad Lib

Figure 2

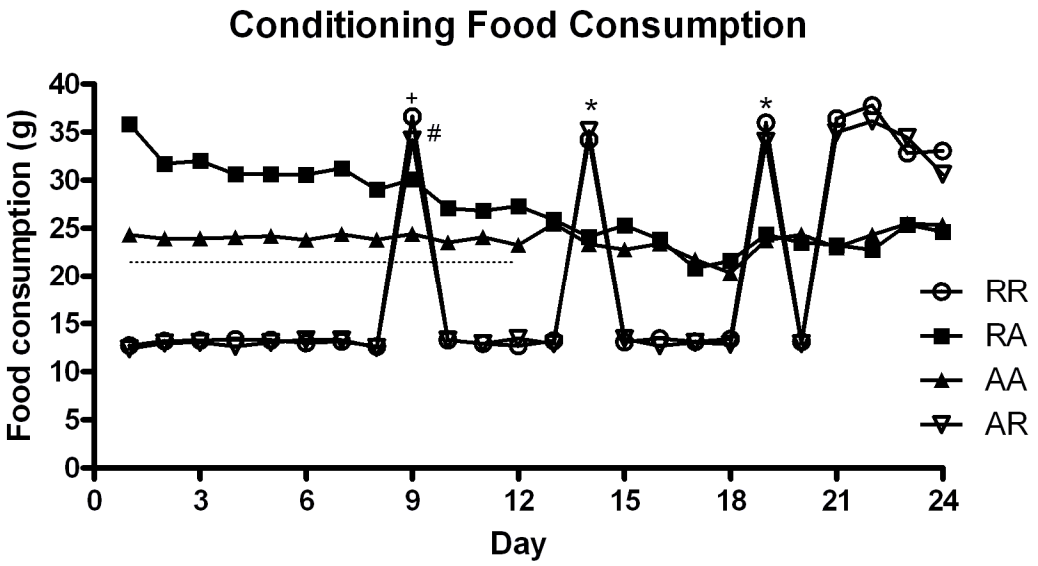

Conditioning Food Consumption
Food consumption (g)
40
35
30
25
20
15
10
5
0
0
3
6
9
12
15
18
21
24
Day
+
#
*
*
RR
RA
AA
AR

Figure 3

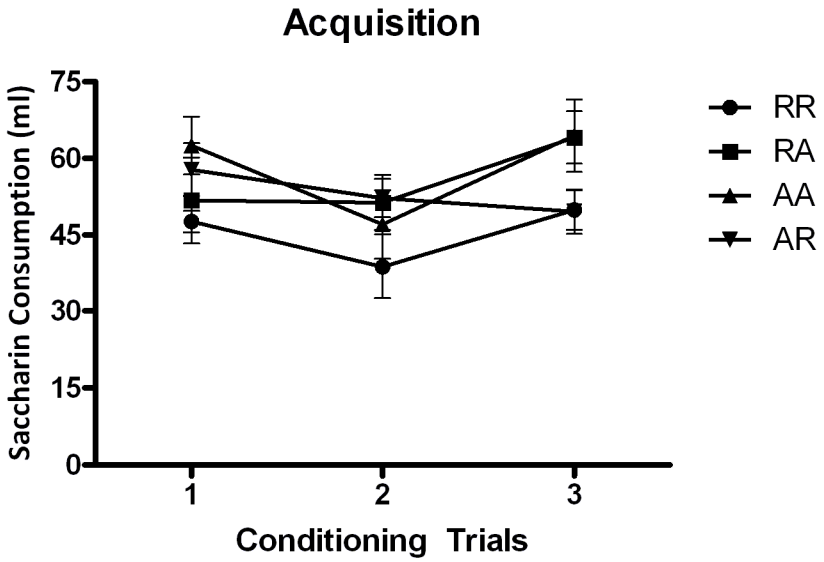

Acquisition
Saccharin Consumption (ml)
75
60
45
30
15
0
1
2
3
Conditioning Trials
RR
RA
AA
AR

Figure 4

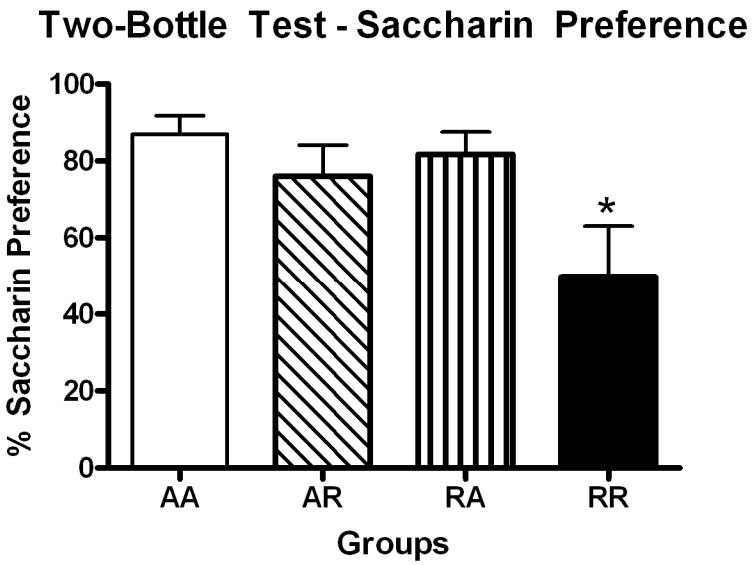
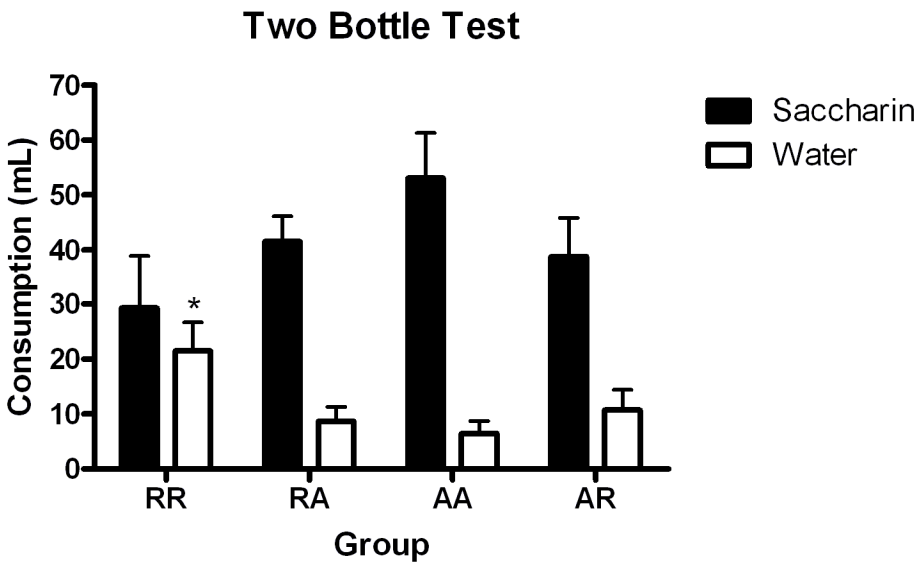

Two-Bottle Test - Saccharin Preference
% Saccharin Preference
100
80
60
40
20
0
*
AA
AR
RA
RR
Groups

Figure 5


Two Bottle Test
Consumption (mL)
70
60
50
40
30
20
10
0
*
RR
RA
AA
AR
Group
Saccharin
Water