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Effect of Maternal Behavior on Anxiety, Resilience, and Memory in Sprague-Dawley Rats

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LONGWOOD
SENIOR THESIS

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Committee Members: Dr. Corey Cleland (James Madison University), Dr. Catherine Franssen (Longwood University), and Dr. Maxwell Hennings (Longwood University).

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by

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This thesis has been read and approved by the following supervisory committee and submitted in its final draft to the Longwood Senior Thesis Committee in the conferment of Honors towards the degree of Bachelor in Biology.

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Abstract

This study seeks to determine the extent that maternal care of rodents influences anxiety levels, memory, and resiliency in the next generation. After categorizing maternal rats as Good and Bad mothers through a pup recognition test, they and their pups were put through a battery of behavioral tasks to assess anxiety (Elevated Plus Maze), memory (Novel Object Preference Test and Object Location Memory Task), and resiliency (Forced Swim Test). Preliminary results found that Good mothers have superior spatial and non-spatial memory in comparison to the Bad mothers. In addition, the pups raised by Good mothers showed greater resilience in comparison to pups raised by Bad mothers based on escape behaviors seen in the Forced Swim Test. This suggests that the type of mother a rodent is (i.e., Good mother or Bad mother) has on effect on their memory and the type of maternal care received by offspring influences resiliency.

Dedication

This Longwood Senior Thesis is dedicated to my parents, Keith and Donna Tignor, who have always encouraged my pursuit of science and have provided me with a passion for learning that made this path possible. I also dedicate this thesis to my roommates, Searra Richardson and Bailey Dallas, and my sister, Lauren Huftalen, without whom I would not have been able to overcome the obstacles of this year.

Introduction

Among the largest concerns in the United States is the rise in mental health disorders. The vast numbers of Americans affected – nearly 1 in 5 adults – has rightfully led to both an increase in the number of researchers working to understand mental health disorders and public support for increasing mental health services in recent years (Kessler et al., 2004; "Mental Illness", n.d.). Among the concerns related to mental health disorders, researchers have determined that mental health issues can contribute to a wide range of physical health issues. For instances, people with mental health disorders are at more risk for communicable and non-communicable disease. Two key neuropsychiatric disorders, anxiety and depression, make up 14% of diseases worldwide (Merikangas et al., 2010). Tragically, anxiety and depression are not limited to adults. In the United States, nearly 1 in 3 adolescents between the ages of 13-18 suffer from anxiety and depression disorders (Merikangas et al., 2010; "Any Anxiety Disorder", n.d.).

With such a large population effect, it is not surprising that researchers are working diligently to understand underlying causes. Research includes studies of parenting styles and hormone expression in the brain during development. For example, findings have been published on the link between mother-daughter relationships and the daughter's anxiety and depression in humans (Crowell et al., 2017) and the relationship between levels of estradiol and progesterone and stress and anxiety (Li and Graham, 2017).

Though valuable, studies conducted in humans have a variety of limitations, including lack of controlled environments and invasive studies of the brain. Because of these limitations, model organisms, such as rats, are also critical in gaining an understanding of the mental health issues that plague people. For instance, controlled studies of ovarian hormone withdrawal (Stoffel et al., 2004) and estradiol treatment for depression in rats (Galea et al., 2001) were precursors to the human experiments described above. In addition, studies such as those from the Kim Lab in Korea suggest that several maternal factors can affect memory, cell survival, and neurogenesis in pups. They found that physical exercise like swimming and running can improve neurological outcomes in rat pups (Lee et al., 2006; Kim et al., 2007). Further, they showed that giving mother rats lipopolysaccharides also improve pup outcomes (Kim et al., 2015). By the very nature of the controlled and sometimes invasiveness of those studies, they could not have been conducted in humans. However, we can extrapolate from previous findings that in addition to direct hormonal and chemical interventions, other effects – such as maternal behavior – can cause changes in the memory of pups.

What's more, evidence suggests that these changes might be passed from generation to generation epigenetically. Research from the Meaney Lab has shown that maternal care is transmitted from one generation to the next. In a series of studies, they showed that an anxious mother rat would raise anxious pups. In turn, those anxious pups would become anxious mothers that would raise another generation of anxious pups. The level of maternal licking and grooming was recorded via methyl tags on the pups' DNA, determining which proteins were translated (Champagne et al., 2003).

Encouragingly, it is possible for cognitive enrichment to take place over the course of one's lifetime. For instance, a variety of studies indicate that significant neurological changes occur when becoming a parent. Focusing on rats, research has found that compared to non-mothers, mother rats have improved spatial and non-spatial memory (Kinsley and Lambert, 2008; Love et al., 2005), improved neuroplasticity (Franssen et al., 2012), and lower levels of anxiety (Massimo et al., 2011; Pawluski et al., 2016). What is unclear is if these neurological effects are passed on to the next generation as well.

This Longwood Senior Thesis project seeks to fill a gap in the literature by investigating the effects of Good or Bad maternal behavior on the cognitive behavior of offspring. Specifically, the aim is to determine the extent that maternal care influences anxiety levels, memory, and resiliency in the next generation at multiple developmental stages.

To do this, techniques and approaches developed in the Franssen Lab at Longwood University were used to identify mother rats as Good or Bad mothers. Previous work has shown that individual rats differ based on a variety of maternal care behaviors, including latency to retrieve pups, grooming, and nursing (Unroe et al., in prep). After classifying the mothers as Good mothers or Bad mothers through a pup recognition test, they and their pups were put through a battery of behavioral tasks, such as the Elevated Plus Maze to assess anxiety, the Novel Object Preference Test to assess non-spatial memory, the Object Location Memory Task to assess spatial memory and the Forced Swim Test to assess resiliency.

Methods and Materials

Animal Subjects and Housing

Pregnant Sprague-Dawley rats (Taconic Biosciences, US) were housed singly in Innovive recyclable cages with ALPHA-Dri® bedding (Innovive, San Diego, CA). There was a total of fifteen (15) pregnant rats with ages ranging from 65-75 days old. Of the fifteen rats, fourteen (14) produced litters and were deemed the parent generation (P). At 35 days-old, pups were weaned from their mothers, males culled, and females sorted into four groups: Pups from Good Mothers (those whose mothers exhibited the fastest maternal retrieval) in Enriched Housing, Pups from Good Mothers in Control Housing, Pups from Bad Mothers (those whose mothers exhibited the slowest maternal retrieval) in Enriched Housing, Pups from Bad Mothers in

Control Housing. Each group had 8 pair housed individuals; this group of 32 female rats became the F1 generation. Prior to testing, one female pup raised by a Good mother with control housing died of unknown causes; the remaining 31 pups went through all the behavioral tests.

Food (Envigio-Teklad 18% Protein rat diet, Envigio Laboratories) and tap water were provided ad libitum to the rats with a 12/12-hour light cycle under standard housing conditions. In individual cages, mothers could give birth and care for pups. All protocols were approved by Longwood IACUC and were in adherence with the Animal Welfare Act and the U.S. Department of Health and Human Services "Guide for the Care and Use of Laboratory Animals".

Behavioral Testing

All fourteen (14) mothers of the P generation were first assessed for maternal behavior when their pups were between 6-9 days old. At 35 days, pups were weaned. Starting one-week post weaning, mothers were tested on four behavioral tests. Pups were tested on the behavioral tests as adolescents, starting at 56 days.

Combined, the behavioral tasks investigated anxiety/boldness, spatial memory, non-spatial memory, and resiliency in the animals. All equipment used during each trial was cleaned with Alconox detergent, wiped with a paper towel, and dried in between trials to use again without the presence of odors from other rats.

Pup Recognition Test

Mothers were tested in 3 groups with different ratios of her own pups (OWN) and pups from another mother (ALIEN). The OWN:ALIEN pup ratio groups were 8:0, 4:4, and 0:8. These ratios had been previously shown to result in different maternal behaviors in the Franssen Lab

(Unroe et al., in prep). To begin the test, mothers were removed from their home cage and placed in a test cage (identical to the home cage, but clean and without food). Her pups were left in the home cage and placed under a heat lamp. After a 5-minute acclimation period in the test cage in the testing room, the appropriate pup ratio was placed in the cage with the mother rat in a Pyrex glass cup: the “Pup Cup”. During the mother’s acclimation period, pups were marked **X** or **II** with an odorless marker to indicate OWN or ALIEN pup and kept under a heat lamp. Since rat pups are poikilothermic, ALIEN pups came from a mother that was not being tested that day and only used for that trial. Eight pups were placed into the Pup Cup and the Pup Cup placed in the test cage with the mother rat. Mothers were then given a 20-minute period to interact with and retrieve pups. This portion of the trial was video recorded for later data analysis. At the end of the trial, the mother and pups were returned to their home cages.

Following all the retrieval tests, lab members analyzed video to classify rats of the P generation as Good or Bad mothers based on average latency to retrieve the 1st pup across the three trials. Time spent interacting with pups (grooming, sniffing, nursing, and nesting) and time spent in non-interaction activities (self-grooming, sleeping, drinking, exploring the cage, sitting, laying, etc.) were also recorded. If the mother was performing an interaction activity and a non-interaction activity simultaneously, the non-interaction activity was counted as the primary activity.

Elevated Plus Maze

Elevated Plus Maze was used to test for anxiety as described in Lezak et al. (2017; Figure 1A). Rats were taken out of home cages, placed in new cage with access to water, and taken to the testing room. After a 5-minute acclimation period to testing room, the rat was placed in center square region of the Elevated Plus Maze apparatus. The trial began immediately and ended after a 5-minute duration. Rats were then returned to their home cages after the 5-minute trial. Video recording of trials were analyzed for time spent by rats in each zone of the apparatus. If the rat was moving from one zone to another, timing for the new zone was started once the rats two front feet entered the arm.

Novel Object Recognition Test

Novel Object Recognition was used to test the rats for non-spatial memory as described by Lueptow (2017; Figure 1B). Rats were taken out of home cages, placed in new cage with access to water, and taken to the testing room. For the first stage of the test, rats were then placed in an open field maze containing two identical objects placed in opposite quadrants of the open field. The rat was given 2 minutes to explore the objects. Following the first stage, rats were removed and returned to their home cage while the testing arena (open field maze) and objects were cleaned and one of the objects was replaced with a new object. For the second, testing stage, the rat was placed back into the maze and allowed 2 minutes to explore both the familiar and new objects. At the end of the second stage, rats were returned to their home cage and the maze cleaned. Using video recordings, researchers logged time spent exploring the familiar and novel objects as a discrimination index. Exploring was classified as sniffing and interacting with the object or area surrounding the object.

Object Location Memory Task

The Object Location Memory Task was used to test the rats for spatial memory as described by Vogel-Cierna and Wood (2014; Figure 1C). Rats were taken out of home cages, placed in new cage with access to water, and taken to the testing room. Rats were then placed in an open field maze containing two identical objects placed in opposite quadrants of the open field. The rat was given 5 minutes to explore the objects. Following the first stage, rats were removed and returned to their home cage while the testing arena (open field maze) was cleaned. In the next stage, the testing stage, one object was left in its original location and one object was placed in a novel quadrant of the open field maze. Ninety minutes after the first stage, the rat was placed in the field and allowed 5 minutes to explore the familiar object location and the novel object location. Using video recordings, researchers logged time spent exploring the familiar and moved objects as a discrimination index. Exploring was classified as sniffing and interacting with the object or area surrounding the object.

Forced Swim Test

The Forced Swim Test was used to test resiliency as described in Commons et al. (2016; Figure 1D). Naïve rats were placed into a tank of twelve inches of water and allowed to swim for 5 minutes. The trial was video recorded for analysis of latency to dive, number of dives, time spent swimming, and time spent floating.

Data Analysis

Each behavioral test was analyzed and scored for the appropriate behavior at the conclusion of each task. At least two researchers scored a sample video in order to achieve inter-rater reliability before scoring the remaining videos. Researchers were blind to whether the rat was classified as a Good mother, Bad mother, pup raised by a Good mother with controlled or enriched housing, or a pup raised by a Bad mother with controlled or enriched housing. Once the behavioral tests were scored for the appropriate behaviors, they were analyzed using an independent samples t-test for Elevated Plus Maze, Novel Object Preference Test, and Object Location Memory Task. The Forced Swim Test was analyzed using a proportion Z-test. For the pup recognition test, retrieval data was compared with the retrieval times of rats from previous studies to determine if the rats in this study were fast or slow retrievers.

Results

Pup Recognition Test

P Generation

Based on latency to retrieve the first pup, some rats quickly retrieved pups regardless of whether they were in the 8:0, 4:4, or 0:8 condition. Others were slow to retrieve or did not retrieve at all. For example, Maternal Rat 3 was the fastest retriever and retrieved the first pup in 13 seconds, while Maternal Rat 12 did not retrieve pups at all. Of the 14 P generation rats, 10 qualified as retrievers and 4 as non-retrievers (Figure 2). This information was used to classify the fastest 10 mothers as Good and the 4 non-retrieving mothers as Bad.

Elevated Plus Maze

P Generation: Post-lactation females

All rats spent significantly less time in the open arms of the maze than the closed arms ($p<0.01$; Figure 3). However, there was no significant difference ($p=0.23$) between the amount of time spent in open vs. closed arm by the Good mothers (M = 65.10, SEM = 15.41, M = 234.90, SEM = 15.41) compared to the Bad mothers (M = 90.75, SEM = 26.56, M = 209.25, SEM = 26.56).

F1 Generation: Adolescent Females

All pups of both Good and Bad mothers spent significantly less time in the open arms of the elevated plus maze ($p<0.01$; Figure 4). Similar to the P generation, there were no statistically significant differences ($p=0.48$) between pups of Good mothers (M = 49.53, SEM = 7.36, M = 250.47, SEM = 7.36) and pups of Bad mothers (M = 42.75, SEM = 5.96, M = 257.25, SEM = 5.96) in the amount of time spent in the open arm vs. the closed arm.

Novel Object Preference Test

P Generation: Post-lactation Females

It was found that Good mothers spent significantly more time ($p<0.05$; Figure 5) investigating the novel object (M = 25.90, SEM = 4.31) than the familiar object (M = 14.00, SEM = 3.82), but Bad mothers did not show a significant difference ($p=0.36$) in the time spent investigating the novel object (M = 26.25, SEM = 5.98) compared to the familiar object (M = 18.00, SEM = 5.76).

F1 Generation: Adolescent Females

Adolescent rats raised by Good mothers ($p<0.05$; Figure 6) spent significantly more time investigating the novel object (M = 22.63, SEM = 3.91) than the familiar object (M = 15.19, SEM = 1.54). The adolescent rats raised by Bad mothers also spent significantly more time ($p<0.05$) investigating the novel object (M = 19.56, SEM = 2.36) than the familiar object (M = 12.09, SEM = 1.45). There were no differences between the groups ($p=0.18$).

Object Location Memory Task

P Generation: Post-lactation Females

When comparing the groups, it was found that Good mothers spent significantly more time ($p<0.05$; Figure 7) with the moved object (M = 52.00, SEM = 8.87) than the stationary object (M = 32.10, SEM = 6.46). However, Bad mothers did not discriminate ($p=0.86$) between the moved (M = 40.25, SEM = 10.21) and stationary objects (M = 37.75, SEM = 10.05).

F1 Generation: Adolescent Females

Adolescent rats raised by Good mothers ($p<0.05$; Figure 8) spent significantly more time investigating the moved object (M = 81.20, SEM = 16.19) than the stationary object (M = 39.20, SEM = 4.48). The adolescent rats raised by Bad mothers also spent significantly more time ($p<0.05$) investigating the moved object (M = 73.65, SEM = 5.58) than the stationary object (M = 44.82, SEM = 5.56). There were no differences between the groups ($p=0.42$).

Forced Swim Test

P Generation: Post-lactation Females

All rats tested swam more than they floated ($p<0.01$), but there was no significant difference between the Good mothers and Bad mothers ($p=0.88$). Rats in each group dove to find an escape from the tank, but a higher percentage of Bad mothers made dive attempts (75%) than Good mothers (30%; Figure 9). However, this result was not statistically significant ($p=0.06$).

F1 Generation: Adolescent Females

Unlike with the post-lactation rats of the P generation, there were significant differences between the groups of the adolescent rats of the F1 generation. There was a statistically significant difference between the percentage of pups raised by Good mothers who attempted dives and pups raised by Bad mothers who attempted dives ($p<0.01$; Figure 10). Of the pups raised by Good mothers, 93% attempted dives and of the pups raised by Bad mothers, 75% attempted dives. Similarly, Adolescent rats raised by Good mothers swam (M = 232, SEM = 6.5) significantly longer ($p<0.01$) than floated compared to the adolescent rats raised by Bad mothers (M = 195, SEM = 8.3; Figure 11).

Discussion

General summary

The current findings of this study represent the beginning of an ongoing, multi-generational, and longitudinal study. As n-values are increased with future trials and generations, more conclusive findings can be expected within each age group. However, in this early stage of research, significant differences between groups are important to note. For instance, differences in memory tasks (Novel Object Preference and Object Location Memory) among the P generation point to variations in memory ability between Good mothers and Bad mothers. Additionally, differences in the Forced Swim Test may be related to maternal care based on the performance of the F1 generation in this task. It is also evident based on the current findings seen between the P generation and F1 generation that developmental stage and motherhood have an effect on spatial and non-spatial memory in the rat model. This is supported by previous research that has found mothers have improved spatial and non-spatial memory compared to non-mothers (Kinsley and Lambert, 2008).

Pup Recognition Test

Among the behaviors tested, it was found that latency to retrieve the first pup in a given trial is a key indicator of Good or Bad mothers. Latency to retrieve the first pup was averaged across 8:0, 4:4, and 0:8 conditions. In order to determine if the rats from this study were fast or slow retrievers, they were compared with times of rats from previous studies (Figure 2). Since it was impossible to know what type of mothers were ordered, the number of Bad mothers was lower than desired (n=4) compared to the number of Good mothers (n=10). The low n-value in the Bad mothers could contribute to the unexpected results from the Elevated Plus Maze and the Forced Swim Test seen in the P generation.

Elevated Plus Maze

As expected, both the P generation of post-lactation rats and F1 generation of adolescent rats spent significantly more time in the open arms than in the closed arms. This is normal for rodents, as previous research suggests that rodents of more cautious in open spaces (Lezak et al., 2017). However, since there were no significant differences between the Good mothers and Bad mothers, preliminary data suggests that the type of mother has no effect on anxiety and boldness. This result is surprising, as it was predicted that Good mothers would be bolder than Bad mothers. However, our prediction is based on the finding that mothers spend more time on open arms than non-mothers - an indication of boldness and low anxiety (Kinsley and Lambert, 2008; Love et al., 2005). Those studies compared mothers to non-mothers and did not compare type of mother (i.e., Good mothers vs. Bad mothers) like this study did. Our findings indicate that motherhood itself may have an effect on boldness and anxiety but once a mother, anxiety is not differentiated at Good/Bad levels. Additionally, the lack of difference seen between the pups raised by Good mothers and the pups raised by Bad mothers in the time spent in open vs. closed arms suggests that the amount and quality of maternal care does not have an effect on boldness and anxiety.

Novel Object Preference Test

In the P generation of post-lactation rats, Good mothers spent significantly more time with the novel object than the familiar object. This finding indicates that the Good mothers have superior non-spatial memory to the Bad mothers. This is consistent with previous work indicating that mothers were better at non-spatial memory than non-mothers (Kinsley and Lambert, 2008; Love et al., 2005).

Unlike in the P generation, the adolescent pups of the F1 generation did not show a significant difference between the groups. This indicates that the amount and quality of maternal care received by the two groups of pups did not have an effect on non-spatial memory. As this project continues and more data are collected across multiple developmental stages it will be interesting to see how this trend could change, especially since the current n-values are small (pups raised by Good mothers: n=12; pups raised by Bad mothers: n=16).

Object Location Memory Task

Similar to the novel object preference test, Good mothers spent significantly more time investigating the moved object, which is consistent with studies that have found that rodents use spatial memory to identify and recall the location of objects (Vogel-Cierna and Wood, 2014). However, the Bad mothers did not show a significant difference in the time spent with each object, indicating that Good mothers are better at identifying the moved object and have superior non-spatial memory to the Bad mothers. This lack of significance seen in the Bad mothers could also be due to the fact that the sample size of Bad mothers consisted of only 4 individuals. With further testing, findings may support the current trend or show that there is no significant difference between Good mothers and Bad mothers in relation to spatial memory as n-values increase.

The adolescent rats of the F1 generation also showed a significant difference in the time spent investigating the moved object than the stationary object; however, there was no difference between the pups raised by Good mothers and the pups raised by Bad mothers. This indicates that the amount and quality of maternal care behavior had no effect on the behavior of the pups when it came to spatial memory. However, this result is based on the analysis of one developmental stage of one generation, so with more data analyzed in future generations, there may be significant differences shown.

Forced Swim Test

When looking at time spent swimming versus time spent floating, the P generation of post-lactation females showed no significant difference between Good mothers and Bad mothers. However, when looking at the dive attempts of the rats, Bad mothers made more dive attempts than Good mothers. Although not statistically significant, there is a strong trend toward significance ($p=0.06$; Figure 9) that would likely be supported with a higher n-value (Bad mothers: $n=4$; Good mothers: $n=10$).

The adolescent rats of the F1 generation did show statistical differences. The higher percentage of dive attempts seen in pups raised by Good mothers may indicate that the Good adolescent rats are making more attempts to escape before they give up. There were also differences seen in swimming versus floating times of the adolescent rats. The pups raised by Good mothers swam significantly more than the pups raised by Bad mothers. Previous research has suggested that floating during the Forced Swim Test might indicate that the animal has given up trying to escape as a passive coping mechanism to conserve energy (Commons et al., 2016). We noted that the rats would swim, then float, then swim again, and so on. When paired with the percentage of animals diving data, it can be concluded that the adolescent rats raised by Good mothers are making greater efforts to escape and therefore exhibiting superior resiliency.

Conclusion and Future Directions

As previously mentioned, this is an ongoing, longitudinal, and multi-generational study. Analysis of more generations of rats will be necessary to accurately assess the effect of maternal behavior on anxiety, memory, and resiliency in their pups. However, preliminary results that show significant differences between groups are important to note. Differences in memory tasks among the P generation point to variations in memory ability between Good mothers and Bad mothers. Not only does motherhood have an effect on spatial and non-spatial memory, but it seems that the type of mother a rodent is (i.e., Good mother or Bad mother) influences memory as well (Kinsley and Lambert, 2008; Love et al., 2005). Moreover, performance of the F1 generation in the Forced Swim Test indicates that resiliency may be related to maternal care.

As this research continues, the F1 generation will be tested on the Elevated Plus Maze, Novel Object Preference Test, Object Location Memory Task, and Forced Swim Test a second time as adults before pregnancy and a third time as post-lactation females. In the summer of 2021, students will continue the project with F2 generation through the PRISM Program. Once the F2 generation in this study have been assessed, more conclusive results on the effect of maternal behavior on offspring can be analyzed.

Acknowledgements

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Figures

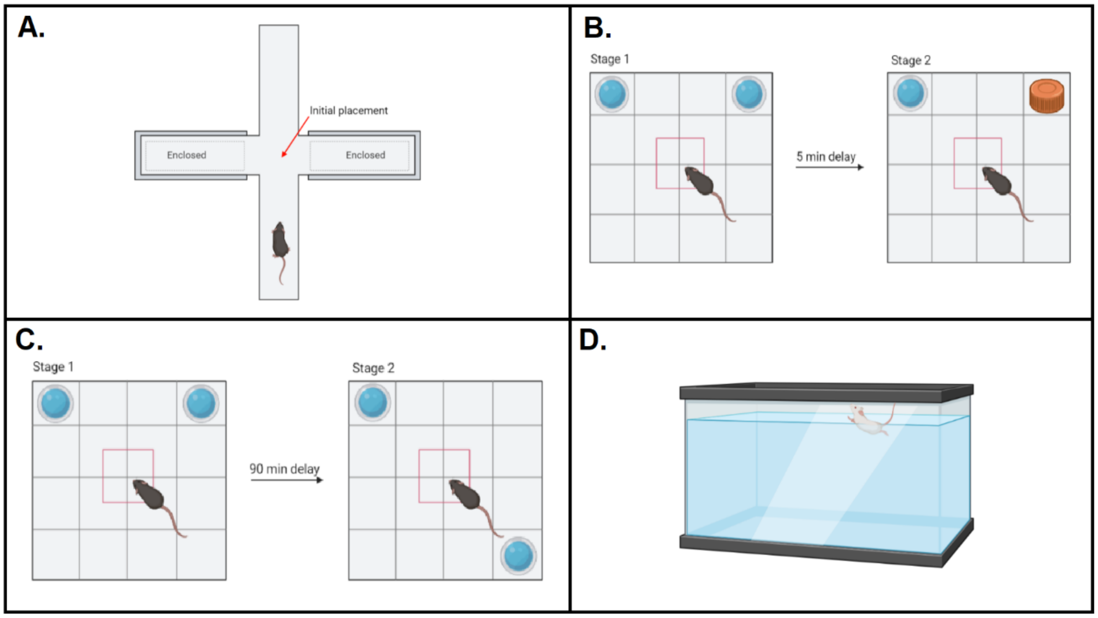

Figure 1. Behavioral apparatuses/tests used in this Longwood Senior Thesis project. Elevated Plus Maze (A), Novel Object Preference Test (B), Object Location Memory Task (C), and Forced Swim Test (D). Created with BioRender.com.

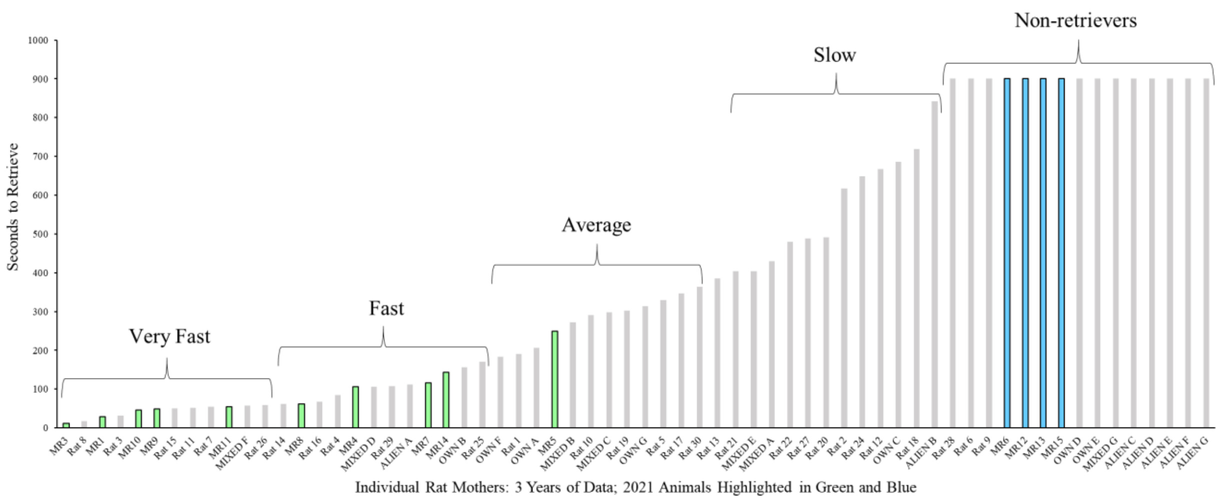

Figure 2. Pup Recognition Test: average latency (seconds) of individual rat mothers to retrieve 1st pup. Rats over three years of data collection represented. Quantiles indicate retrieval speed (i.e., very fast, fast, average, slow, and non-retrievers). Green indicates latency of maternal rats from 2021 classified as Good mothers, blue indicates latency of maternal rats from 2021 classified as Bad mothers, grey indicates maternal rats tested in previous studies in the Franssen Lab.

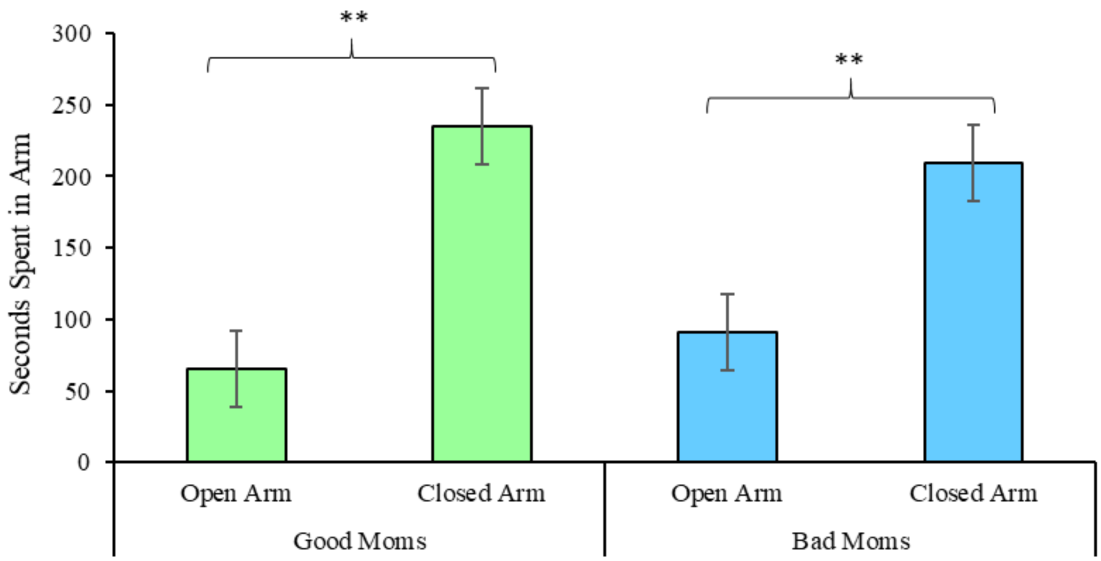

Figure 3. Elevated Plus Maze: time spent (seconds) for each group of post-lactation female rats in P generation (Good moms and Bad moms) in open and closed arms of elevated plus maze. **p<0.01; independent samples t-test; Good mothers: n=10; Bad mothers: n=4; error bars ± SEM.

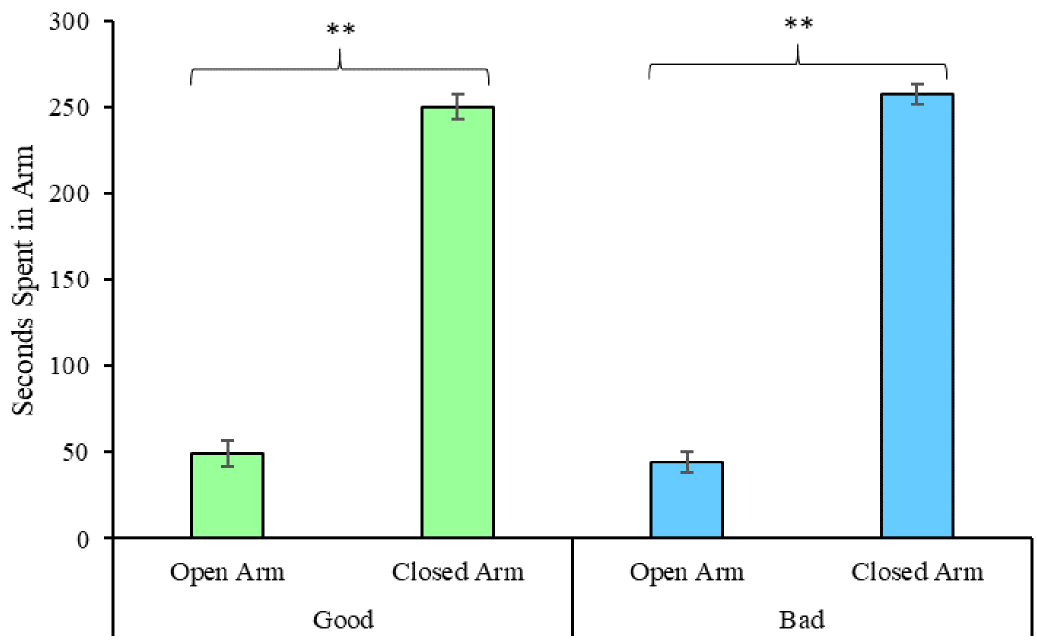

Figure 4. Elevated Plus Maze: time spent (seconds) for each group of adolescent females of the F1 generation (pups raised by Good moms and pups raised by Bad moms) in open and closed arms of elevated plus maze. **p<0.01; independent samples t-test; Good raised rats: n=15; Bad raised rats: n=16; error bars ± SEM

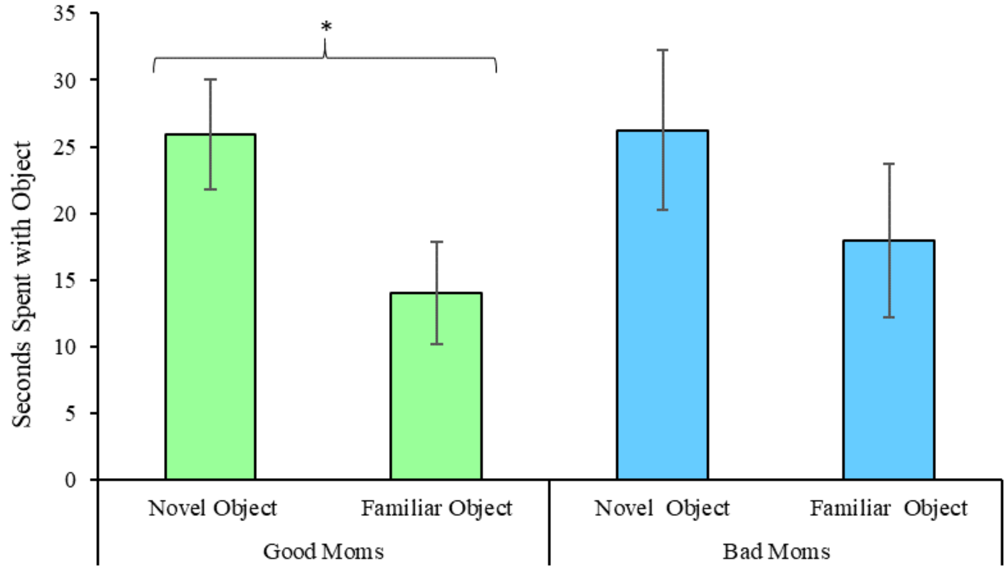

Figure 5. Novel Object Preference Test: time spent (seconds) for each group of post-lactation female rats in P generation (Good moms and Bad moms) investigating novel object and familiar object. *$p<0.05$; independent samples t-test; Good mothers: n=10; Bad mothers: n=4; error bars ± SEM.

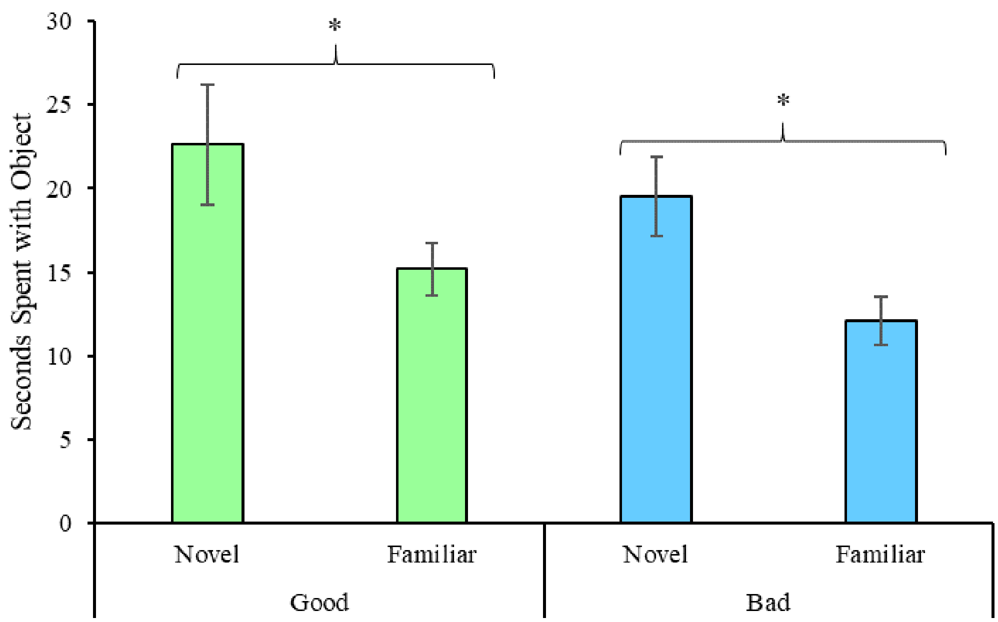

Figure 6. Novel Object Preference Test: time spent (seconds) for each group of adolescent females of the F1 generation (pups raised by Good moms and pups raised by Bad moms) investigating the novel object and the familiar object. *$p<0.05$; independent samples t-test; Good raised rats: n=12; Bad raised rats: n=16; error bars ± SEM.

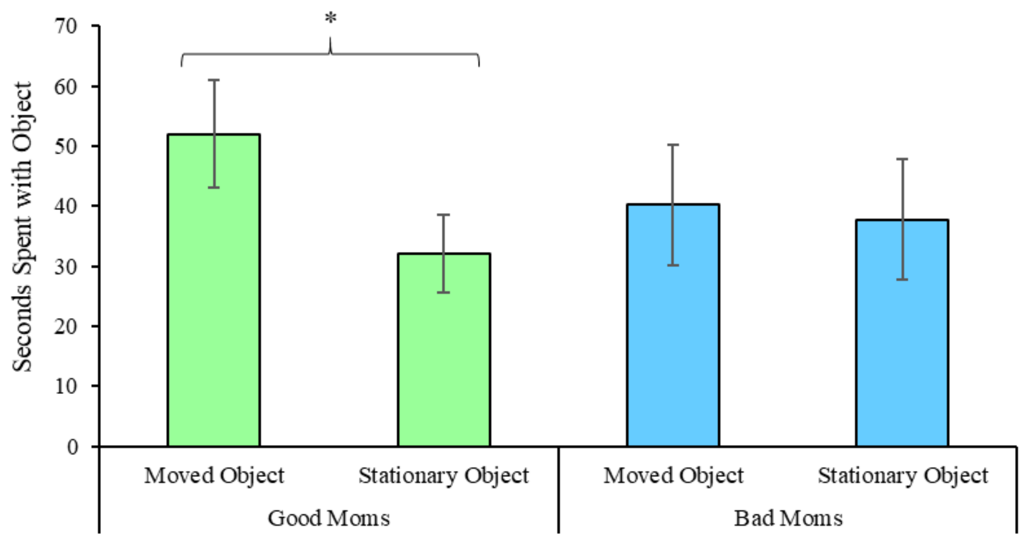

Figure 7. Object Location Memory Task: time spent (seconds) for each group of post-lactation female rats in P generation (Good moms and Bad moms) investigating moved object and stationary object. *$p<0.05$; independent samples t-test; Good mothers: n=10; Bad mothers: n=4; error bars ± SEM.

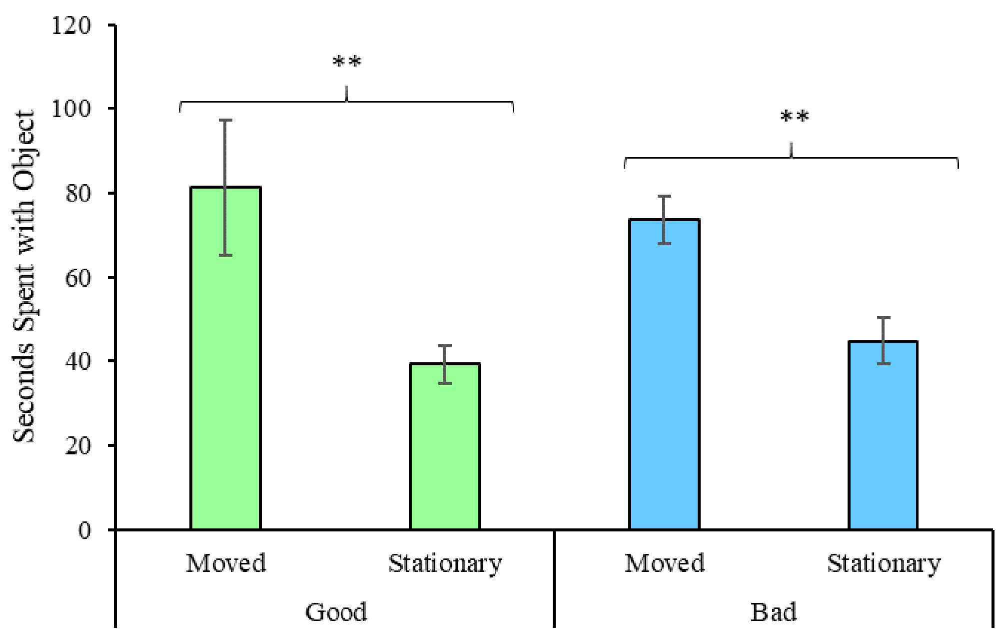

Figure 8. Object Location Memory Task: time spent (seconds) for each group of adolescent females of the F1 generation (pups raised by Good moms and pups raised by Bad moms) investigating the moved object and the stationary object. **$p<0.01$; independent samples t-test; Good raised rats: n=15; Bad raised rats: n=16; error bars ± SEM.

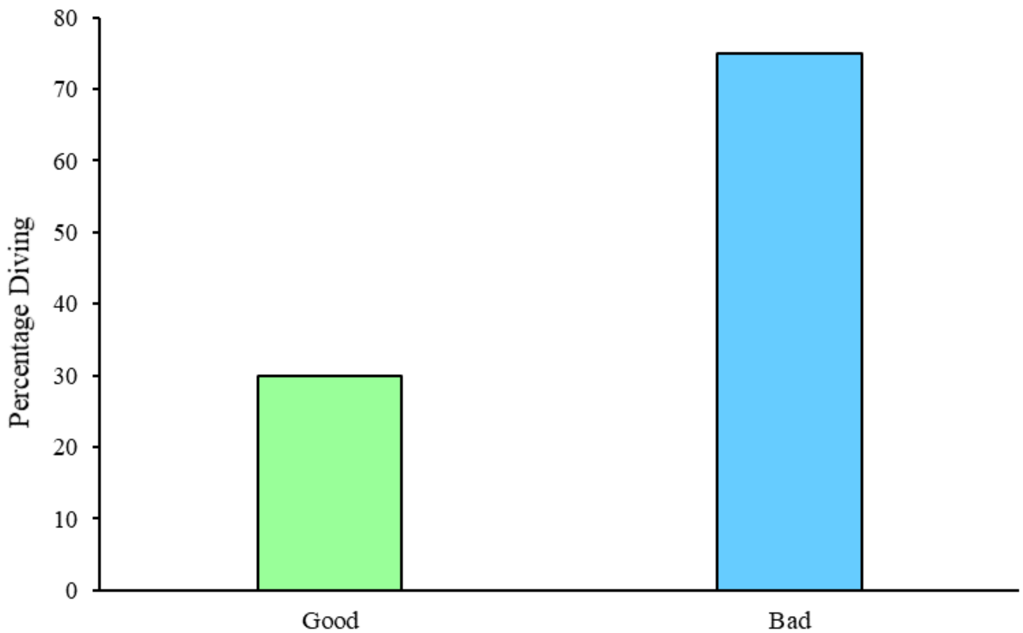

Figure 9. Forced Swim Test: percentage of each group of post-lactation female rats in P generation (Good moms and Bad moms) that made a dive attempt during the forced swim test. p=0.06; proportion Z test; Good mothers: n=10; Bad mothers: n=4.

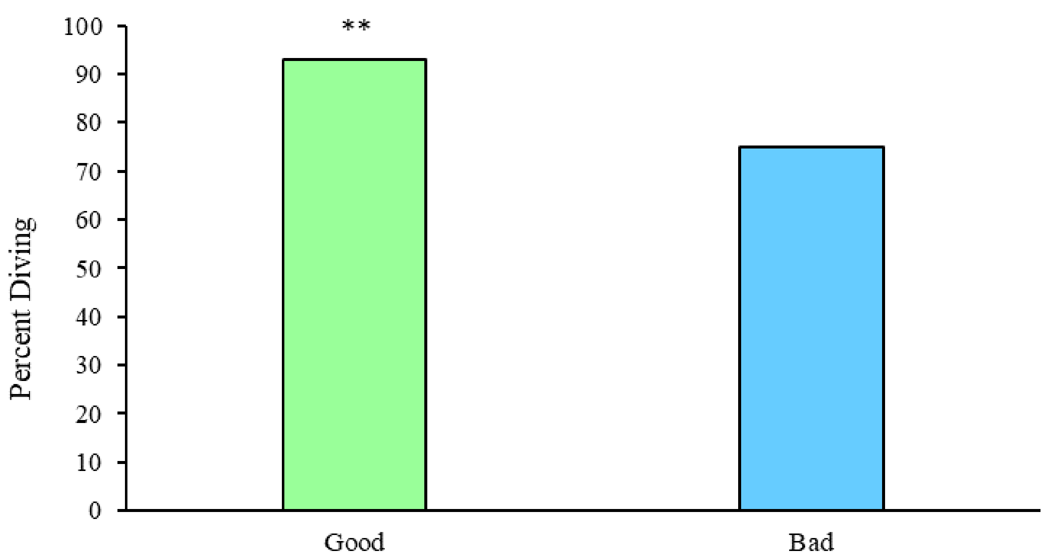

Figure 10. Forced Swim Test: percentage of each group of adolescent females of the F1 generation (pups raised by Good moms and pups raised by Bad moms) that made a dive attempt during the forced swim test. **$p<0.01$; proportion Z test; Good raised rats: n=14; Bad raised rats: n=16.

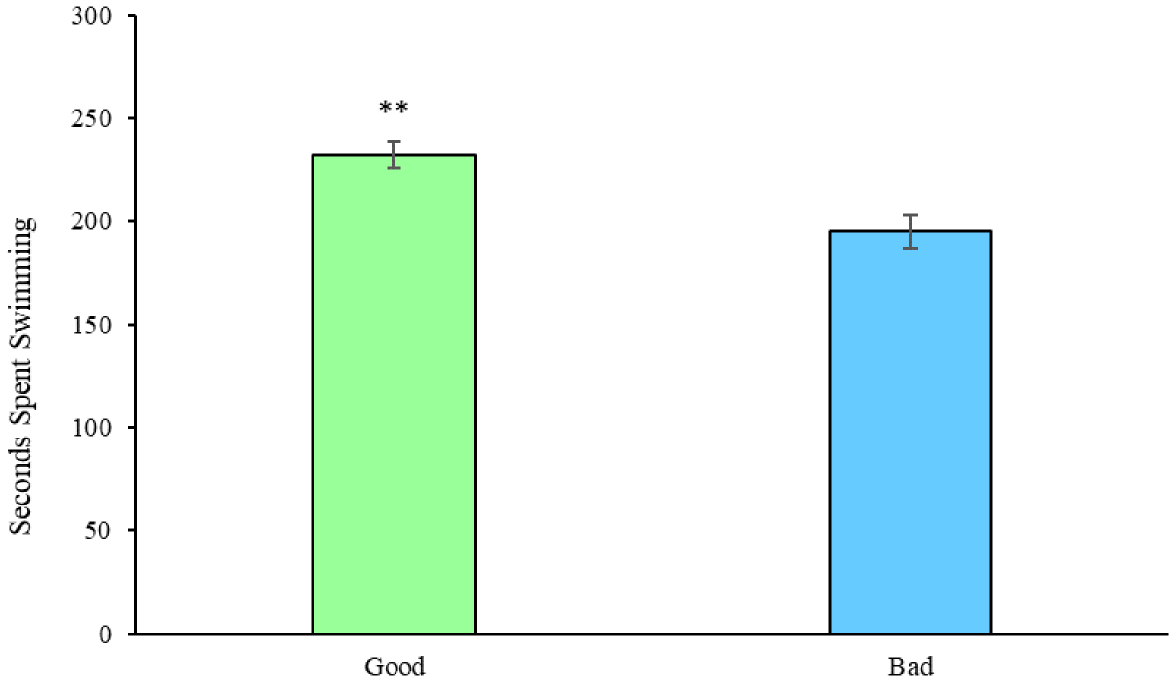

Figure 11. Forced Swim Test: time (seconds) spent swimming of each group of adolescent females of the F1 generation (pups raised by Good moms and pups raised by Bad moms) during the forced swim test. **$p<0.01$; proportion Z test; Good raised rats: n=14; Bad raised rats: n=16.