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EXPLORING THE LINK BETWEEN GENETICS, CHRONIC STRESS, AND DEPRESSION

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ABSTRACT
Depression is a very debilitating mental illness that affects about 7% of the American Population [1] and up to about 350 million people worldwide [2]. Several studies have attempted to find genetic associations with depression in human populations [3]. A strong association between chronic uncontrollable stress and depression has been found [4].

INTRODUCTION
Depression affects about 7% of the American Population [1] and up to about 350 million people worldwide [2]. Several studies have attempted to find genetic associations with depression in human populations [3]. A strong association between chronic uncontrollable stress and depression has been found [4]. In order to assess the effects of genes and stress in mice we have used genetically engineered mice in a learned helplessness paradigm.

cFos is a gene that is immediately expressed upon neuronal activation (Immediate Early Gene). Comparison of cFos positive neuron numbers in similar brain regions in genetically modified (HET) and control mice (WT) can give insights into the brain regions responsible for the depressive phenotype [5]. Certain areas of the brain have been shown to be of higher interest in relation to learned helplessness, including: the medial prefrontal cortex, dorsal hippocampus, and the amygdala [6].

METHODS
- Male mice were genotyped via PCR from tail biopsies and split into two groups, HET (n=10) and WT (n=8) littermates.
- The forced swim test was modeled after Stone and Lin [7] (2011). Each mouse was placed into a 44 x 24 x 21 cm tank, filled with 10 cm high water at 32-34ºC.
- Mice were forced to swim for 15 minutes a day for a total of four days, and immobility time was recorded during these trials.
- On the fourth day, an hour and half after the mice finished the trial, they were deeply anesthetized and perfused with paraformaldehyde to preserve the brains.
- The brains were removed and sliced at 50µm.
- Stained brain slices were examined using a confocal microscope in order to tell where the cFos+ neurons are present and how many of neurons were activated.
- Images of specific brain regions were acquired and examined in photoshop to count the number of cFos activated cells. This is done by dividing pictures into square grids and counting number of activated cell per square.

RESULTS
Behavioral results:
Current results from the forced swim test show that HETS show more immobility time WT mice (Figure 1) (HET n = 10; WT n = 8). T-test analysis of percent immobility of WT and HET mice revealed a p-value of 0.099, therefore the results are not statistically significant. More mice will be tested in the future in order to increase statistical power.

![Figure 1: Average Immobility Time](image1)

Average Immobility Time

<table>
<thead>
<tr>
<th>Geotype</th>
<th>% Time in Immobility</th>
</tr>
</thead>
<tbody>
<tr>
<td>WT</td>
<td>52.5</td>
</tr>
<tr>
<td>HET</td>
<td>57.2</td>
</tr>
</tbody>
</table>

Figure 2: cFos expression (green) in the Mouse Dentate Gyrus during the Forced Swim Paradigm. Neurons are labeled red using Neurotrace.

![Figure 2](image2)

cFos Activated Cells:
We have completed the analysis of cFos immunostaining in the dorsal hippocampus. Images were captured on a Zeiss 710 confocal microscope. cFos positive cells from the upper lip of the Dentate Gyrus of the mouse Hippocampus were counted (2 images per animal). The average activated cells in HETS was found to be 45.8 while in WTS 37.3 (Figure 2). A 2-tailed t-test was done on the two groups mice and found a p-value of 0.32. Therefore, there was no significant difference between the two genotypes in neuronal activation in the dentate gyrus region. Other sections of the brain, including the amygdala and the orbital frontal cortex, are currently being counted and analyzed.

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REFERENCES