May 14, 2014

Today was the first day of my summer internship at Columbia University's Medical Center working in the neurobiology lab of Dr. René Hen! My mentor for the summer is studying specific neural projections from the ventral hippocampus to the amygdala and their effects on memory and anxiety, specifically in a mouse model. Over the course of this summer, I will be learning the basic techniques used by members of this lab to handle mice and analyze brain images. Hopefully, I will also have time to conduct a mini-experiment independently.

I started off the day jumping head first into mouse work. My mentor Jessica had to perform a procedure called perfusion on several mice she had already run in behavioral experiments. This means she already had behavioral data from each of the mice in the context of certain environments that allowed her to test different aspects of memory or anxiety. Perfusions would now allow her to remove their brains and collect physiological data about the strength of neuronal connections in specific areas.

In order to “harvest” a mouse brain that can later be examined under a microscope, it must first be cleared of all blood and other bodily fluids that might obstruct the view of the brain. In addition, because the brain is organic material, it must be preserved so it is impervious to decay. These are the two main goals of perfusions. First, the mouse is sacrificed, then all the blood is pumped out of its body and replaced with a buffer solution, and finally the body is frozen with formaldehyde. After all this is done, the brain can be removed from the mouse’s head and placed in a sucrose solution to prevent growth of bacteria and continue preservation of the tissue.
As you can imagine, this process is rather graphic for someone who has never even worked with mice in a laboratory setting. I was definitely a bit queasy watching this process, and I felt terrible for each mouse that was placed on the operating table. It took a great deal of convincing from Jessica before I finally consented to try a perfusion on my own.

Though today was definitely out of my comfort zone, at the end of the day I felt accomplished for having learned a difficult procedure I had never imagined I would have to perform. When she could see I was struggling, Jessica made sure to point out that the mice couldn’t feel a thing because of the anesthesia and drugs we had injected prior to the perfusions. In addition, she continually reminded me to focus on the big picture. Who knows what our experiments, incomplete without this pivotal step, might tell us about brain circuits involved in memory formation or anxiety prevention and the implications for the progress of human health and medicine. This learning experience was a great kickoff for my summer in the lab and I cannot wait to get started.

May 20, 2014

The first week of my internship has flown by. After the first day, things got a little less graphic, but I’ve still been learning completely new and interesting lab procedures everyday.

Today I mainly practiced a technique I learned last week, slicing harvested brains to be mounted on slides. Although there is a machine that does the actual slicing, it is operated by hand and this is actually a very delicate procedure. The brains are first encased in a frozen chemical and then must be kept within a very specific temperature range to prevent the casing from melting. In addition, we have to cut brain slices that are only 55 microns thick, which is much smaller than even the head of a pin. This means that they can rip very easily or disappear entirely if dropped. A great deal of precision is also involved in making sure the brain is
positioned exactly perpendicular to the blade so that all the slices added together can depict an even, step-by-step view of the brain.

Though I came into this internship expecting to be challenged, I didn't necessarily realize that so many of my challenges would be manual or require such meticulousness. Because there are so many little steps that must be taken to even begin collecting physiological data, each step must be as close to perfect as possible in order to minimize overall error in the experiment. I think working in a lab probably necessitates a good balance between being extremely careful and still getting things done: if you are too much of a perfectionist then you won't make any progress; however, if you work too quickly then you are apt to make careless mistakes.

June 2, 2014

Over the past few weeks I have been learning and practicing mainly data collection techniques. Today, however, my mentor informed me that I'm going to get to run a small experiment soon! She is trying to introduce a new kind of behavioral test to her experiments, but because the mice she uses are optimized for optogenetics, she needs to see if this test works on normal mice first. We met today to discuss if I would be interested in taking on this project in the upcoming weeks. A few of her mice just had litters and as soon as the pups are old enough, we will be able to start. This will give me some time to read some related studies and figure out an experiment design compatible with our lab’s technology and our specific goals.

June 20

Though I am still waiting for the mice to grow old enough, I have still been very busy with the brains we harvested the first week of my internship. After harvesting and slicing all of the brains, the next step in the process is to stain the tissue so certain areas of interest will be lit up when we look at the brain under a microscope. There
is a whole science behind this, called histology, but I only know a few fundamentals. 
In order to make these areas light up, we have to stain the tissue twice with two 
different solutions. Basically, the first solution contains tags that will stick to our 
specific regions of interest. The second solution contains a different set of colored 
tags that will stick to the first kind of tag and this is how the tissue will later show up 
as colored. Once the brain is stained, it can be mounted onto a slide and looked at 
under a microscope.

Today and the past few days, I have been studying these newly mounted slides on a 
high power laser microscope. For every set of brain slices, I have been locating a 
specific section of the amygdala, a center in the brain that plays a large part in 
emotional responses and whose abnormalities have been linked to anxiety and 
phobias. Once I locate the amygdala, I have to take pictures of it in 20x 
magnification. Later, these pictures will be used to count the number of neurons and 
the number of specially stained neurons in order to yield quantitative data. I think 
this is the least challenging step in the process so far and it’s been nice to kind of 
slow things down and relax a little.

July 1, 2014

I had another one-on-one meeting with my mentor today so we could finalize some 
plans for the experiment I’m running this month. My mentor wants to see what role 
the specific projections she is studying have in mice when it comes to predator fear 
associations. Because a predator fear conditioning test has never been run in our 
lab, we want to design and test a protocol to make sure it works before we run any 
tests on her special mice.

Predator fear conditioning is based on a mouse’s natural, innate aversion to 
predator scents. The idea is that if a mouse is familiar with a certain environment, 
and all of a sudden a predator scent is introduced to that environment, the mouse 
will start to behave differently, perhaps moving faster or avoiding the source of the
scent. In addition, if the mouse is placed in the exact same environment at a later
time, it will remember the predator scent and act differently than it did before the
scent was introduced. One specific behavior that supposedly increases is called
freezing, where the mouse's entire body will become very still and it won't move at
all. My experiment will hopefully verify that freezing increases within our set
paradigms.

Today we decided on the specific layout of our environment, which will be in a
3ftx3ft box. The scent will be placed in the middle of the box the third time each
mouse encounters the box. We chose to use coyote urine as our scent and this
makes me a little nervous because it's supposed to be very pungent! I really hope it
won't make me smell like coyote pee. We also figured out the number of times each
mouse will be in the box and how much time they will spend in the environment for
each round. I am very excited for this experiment to begin, especially because I will
be running it on my own. I am looking forward to the added responsibility and I
hope the experiment goes well.

July 1

The mice we'll be using for our experiment are almost old enough now! I have been
handling them for the past few days in order to get them more used to me. This just
means holding them and letting them crawl on my (gloved) hands. Just today, my
mentor taught me how to “scruff” them.

Scruffing a mouse is a particular way of holding a mouse so that it freezes and
cannot bite you. Mice are used to getting picked up by the nape of their neck because
the mother will do this a lot when they are pups and can’t really move a lot on their
own. Scruffing a mouse is basically just holding them by the back of their neck, and
this is actually a very relaxing position for them so they will freeze. This technique is
necessary for her experiments because she needs them to be still so she can attach
cables to their heads when she runs behavioral tests.
Although I probably won’t be scruffing the mice I use in my experiment, getting to practice helped me become much more comfortable handling the mice and I think they are more comfortable with me as well. This will also contribute to the validity of my experiment. If the mice aren’t familiar with me, they might see me as a potential predator and this could confound the results.

The mice will be old enough in about a week, and I can’t wait to start my experiment!

July 12, 2014

Today, I am exhausted. I had to be at the top of my game and extremely focused all day because I was the only person in the lab on a Saturday and it was the very first day of actually conducting my experiment.

Overall, I think the trials went smoothly and there were only a few small errors that I will have to be mindful of tomorrow when I run the second round. None of my tasks were particularly difficult but there was a lot of things I had to remember exactly how to do, from setting up the environment box and recording technology, to making sure all the mice were separated and labeled, to how each mouse should be put into the box and when, to making sure everything was put away and cleaned at the end of the day. I wanted to make sure I wrote about today since it is probably the most important day of my internship; however, I have another long day ahead of me tomorrow so this entry will have to be rather short.

July 17, 2014

This is my last journal entry because my internship is ending tomorrow. It has been such an incredible summer and I feel like I have learned so much. Though I have worked in labs before, it was definitely a completely different experience because I
have never worked full time and had this amount of responsibility. My favorite part of the internship was probably seeing an experiment through from beginning to end; this made me feel very accomplished and like I created something tangible with all of my time. Although the results from my experiment have yet to be fully analyzed, so far our statistical analyses suggest that the protocol worked and the mice behaved like they were supposed to! I had such a great experience conducting neurobiological research that I plan to stay on with the same lab this fall. I am definitely sad to be leaving New York in a few days, but I cannot wait to be back soon!