Male versus Female Brain

Teacher Instructions

Core Concepts:

- Overall male and female brain form and function is very similar, however, on average there are some differences that may explain differences in the rates of some neurological diseases in male and females.
- Endocrine glands secrete hormones that act throughout the body including the brain

Class time required:

Approximately 2 X 40 minute class periods if part 1 is done as a pre-lab, parts 2, 3 and 5 are done in class and parts 4 and 6 are done as homework.

Teacher Provides:

For ALL PARTS each student will need

- Copy of student handout

For Part 3 each team of 2-4 students:

- Copy of **Brain Map** (black and white printed on paper)
- Copy of **Female Brain Map Overlay** (printed in color on transparency)
- Copy of **Male Brain Map Overlay** (printed in color on transparency)

For Part 5 each team of 2-4 students:

- Bag or bin containing:
  - 1.5 ml microtubes or other small tubes prepared as shown in the chart below:

Label on Tube	Contents of Tube – 1 mL of
Jack 3 month old male	pH 9 buffer
Jill 3 month old female	pH 6 buffer
Testosterone Test Solution	0.01% Bromothymol blue solution

  - Droppers labeled:
    - Jack 3 mo old male
    - Jill 3 mo old female
    - Testosterone Test Solution
  - **Hormone Test Sheet** (page 5)printed on plastic transparency sheets
  - Small bag labeled "**Estrogen Test Paper**" containing at least 5 small pieces (cut paper into pieces that are about ½ inch long) of pH 1-12 test paper.

- **Testosterone and Estrogen Color Charts** (page 6).Consider laminating for use by multiple classes.

For Part 6 each team of 2-4 students:

- Copy of **Hippocampus Neuron** (printed in color on paper)
- Copy of **Amygdala Neuron** (printed in color on paper)
- Copy of **Testosterone Signal Pathway Overlay** (printed in color on transparency)

Suggested Class Procedure

1. Assign **Part 1** "**Don't get Testy**"**…** handout for homework or discuss as a group as a pre-lab activity

2. Do **Part 2** in class with each student completing the tests on their own

   In this activity students will take one or two short memory tests that have been reported to show male/female differences.

   The first test is the California Verbal Learning Test (CVLT) a **verbal memory test** in which a list of 16 words (a grocery list) is read aloud to the class. After a pause of 1 minute (or longer) of time students are asked to write down as many of the words as they can remember. The total number of correct words is then tallied.

   http://www.memorylossonline.com/glossary/californiaverballearningtest.html

   The second **spatial memory test** is a that tests spatial memory through a spatial rotation test. Students are provided with a complex 2 dimensional image and then must determine which of three possible choices represents the same object rotated in any of three dimensions. This is considered a memory task as one must keep the original image in their mind as they compare it to the other available options.

3. Perform **Part 3** as students work in small groups. Students will learn some brain anatomy as they determine which regions of the brain differ in size on average between males and females.

4. Have students complete **Part 4 "Neurological Diseases in Males and Females**" as homework or in class. This section provides students with a table of data on the rates of neurological diseases in males and females. Alzheimer's disease is not included as the difference in Alzheimer's incidence in males and females (higher in females) is due to the greater lifespan of females. Males and females of the same age have the same rate of Alzheimer's incidence.

Important Note: The fact that there are NO neurological diseases which ONLY affect males or ONLY affect females indicates that there is **considerable overlap in the form and function of male and female brains.**

5. Complete **Parts 5 "Hormones and the Brain"**

   Distribute the following materials to each team when students begin Part 5.

   - Droppers and tubes labeled:
     - Jack 3 mo old male
     - Jill 3 mo old female
     - Testosterone Test Solution
   - **Hormone Test Sheet**
   - Small bag of "Estrogen Test Paper"
   - **Testosterone and Estrogen Color Chart**

6. Part 6 "**Sorting Out The Signals**" as students work in small groups.

   In this part the students will use short reading passage and a simple model to develop their understanding of how hormones can affect neurons. Specifically they will examine the steps that occur in two different brain neuron types from testosterone binding, to transcription, to translation, and cellular effects.

7. Provide **Part 7 "Bias-ology**" as homework or discuss in class.

Additional information/resources

Here is a link to a 2012 article by McCarthy et al entitled, "Sex Differences In The Brain: The Not So Inconvenient Truth"
http://www.jneurosci.org/content/32/7/2241.full

This is an article from 2005 in Scientific American written by Larry Cahill, Professor of Neurobiology at the University of California of
http://www.bio.uci.edu/public/press/2005/hisherbrain.pdf

Part 2 Teacher Instructions for memory tests

Test #1 Verbal memory (*Females on average tend to perform better at this memory task)*

1. Read the list of words below entitled, “Monday’s Shopping List” to the students at a normal pace.
2. Have students wait one minute after the last word is read.
3. Allow students 1 minute to write down all the words they remember in **the student data table**.
4. After 1 minute of writing, read the list aloud again and have students mark all the correct words that they listed.
5. Have students calculate the total number of words they correctly remembered in the space provided on the table.
6. Class averages for males and females can be tallied and, if desired, graphed.

Monday’s Shopping list

1. **Apples**
2. **Bananas**
3. **Grapes**
4. **Oranges**
5. **Pepper**
6. **Salt**
7. **Sugar**
8. **Cinnamon**
9. **Cheese**
10. **Milk**
11. **Yogurt**
12. **Butter**
13. **Ham**
14. **Turkey**
15. **Ground beef**
16. **Chicken**

Test #2 Spatial Memory Test (*Males on average tend to perform better on this test*)

1. Hand out the spatial rotation tests to the students face down.
2. Students should be instructed that for each image on the left side of the page there are two images on the right side which represent the SAME object rotated in some direction.
3. Students must correctly identify BOTH of the correct answers for the question to get credit for that question.
4. Allow 5 minutes for the students to answer the questions.
5. Review the correct answers with the students and have them record the total number correct.
6. Class averages for males and females can be calculated and if desired, graphed.

For Part 5

Hormone Test Sheet *(print on transparency sheet)*

Hormone Test Sheet	Testosterone Test	Estrogen Test
Jack 3-month old male	○	□
Jill 3-month old female	○	□

Hormone Test Sheet	Testosterone Test	Estrogen Test
Jack 3-month old male	○	□
Jill 3-month old female	○	□

Hormone Test Sheet	Testosterone Test	Estrogen Test
Jack 3-month old male	○	□
Jill 3-month old female	○	□

Hormone Test Sheet	Testosterone Test	Estrogen Test
Jack 3-month old male	○	□
Jill 3-month old female	○	□

Testosterone Test Color Chart		Estrogen Test Color Chart	
Testosterone Level	Color	Estrogen Level	Color
0-5		0	
6-10		1	
11-50		2	
51-100		3	
101-200		4	
201-300		5	

Testosterone Test Color Chart		Estrogen Test Color Chart	
Testosterone Level	Color	Estrogen Level	Color
0-5		0	
6-10		1	
11-50		2	
51-100		3	
101-200		4	
201-300		5	

Testosterone Test Color Chart		Estrogen Test Color Chart	
Testosterone Level	Color	Estrogen Level	Color
0-5		0	
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101-200		4	
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Testosterone Test Color Chart		Estrogen Test Color Chart	
Testosterone Level	Color	Estrogen Level	Color
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6-10		1	
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Testosterone Test Color Chart		Estrogen Test Color Chart	
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0-5		0	
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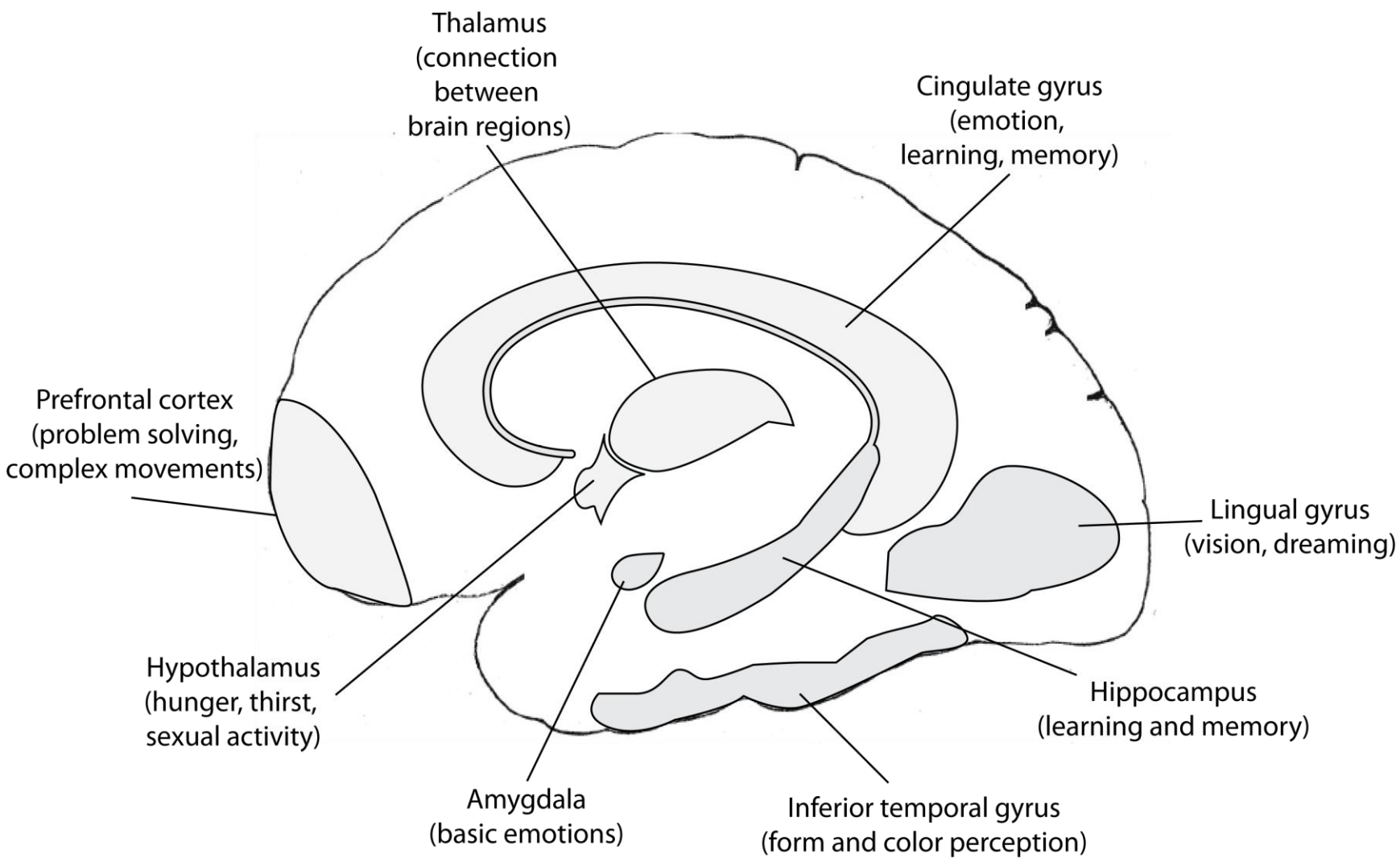
201-300		5	

Testosterone Test Color Chart		Estrogen Test Color Chart	
Testosterone Level	Color	Estrogen Level	Color
0-5		0	
6-10		1	
11-50		2	
51-100		3	
101-200		4	
201-300		5	

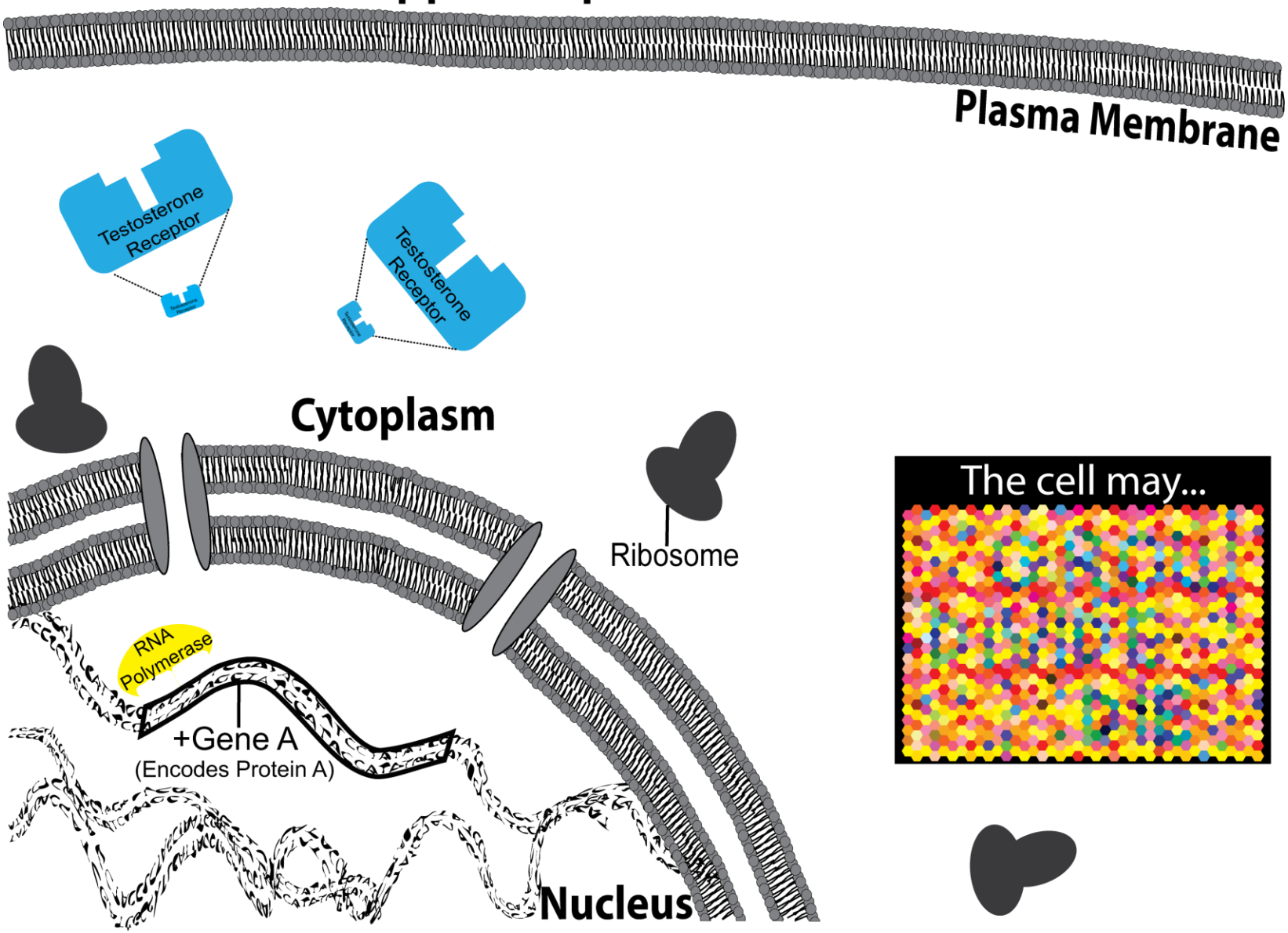
For Part 3 (*print on regular paper*)

Brain Map

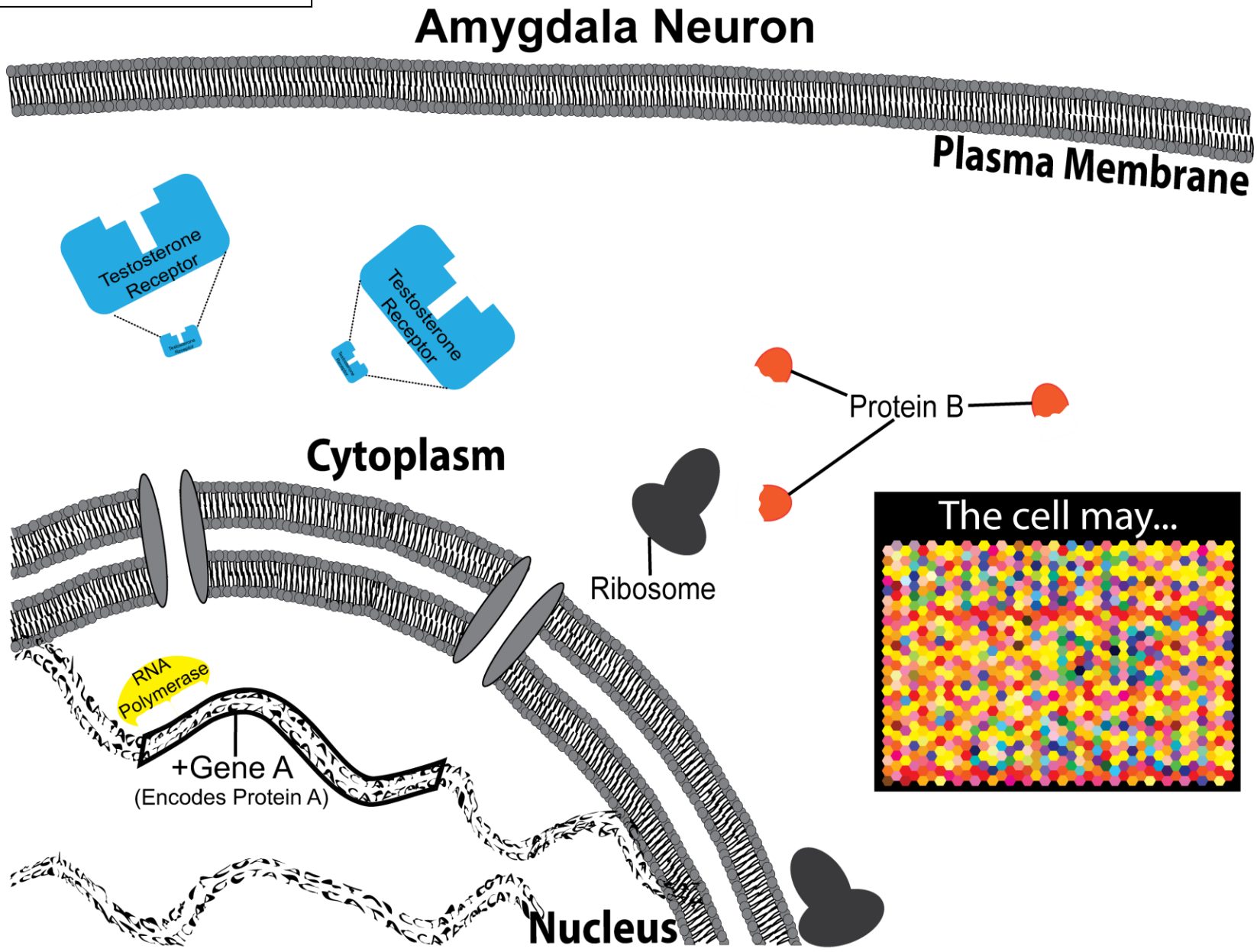


For Part 6 (*print on regular paper*)

Hippocampus Neuron



For Part 6 (*print on regular paper*)



For Part 3 (*print on transparency*)

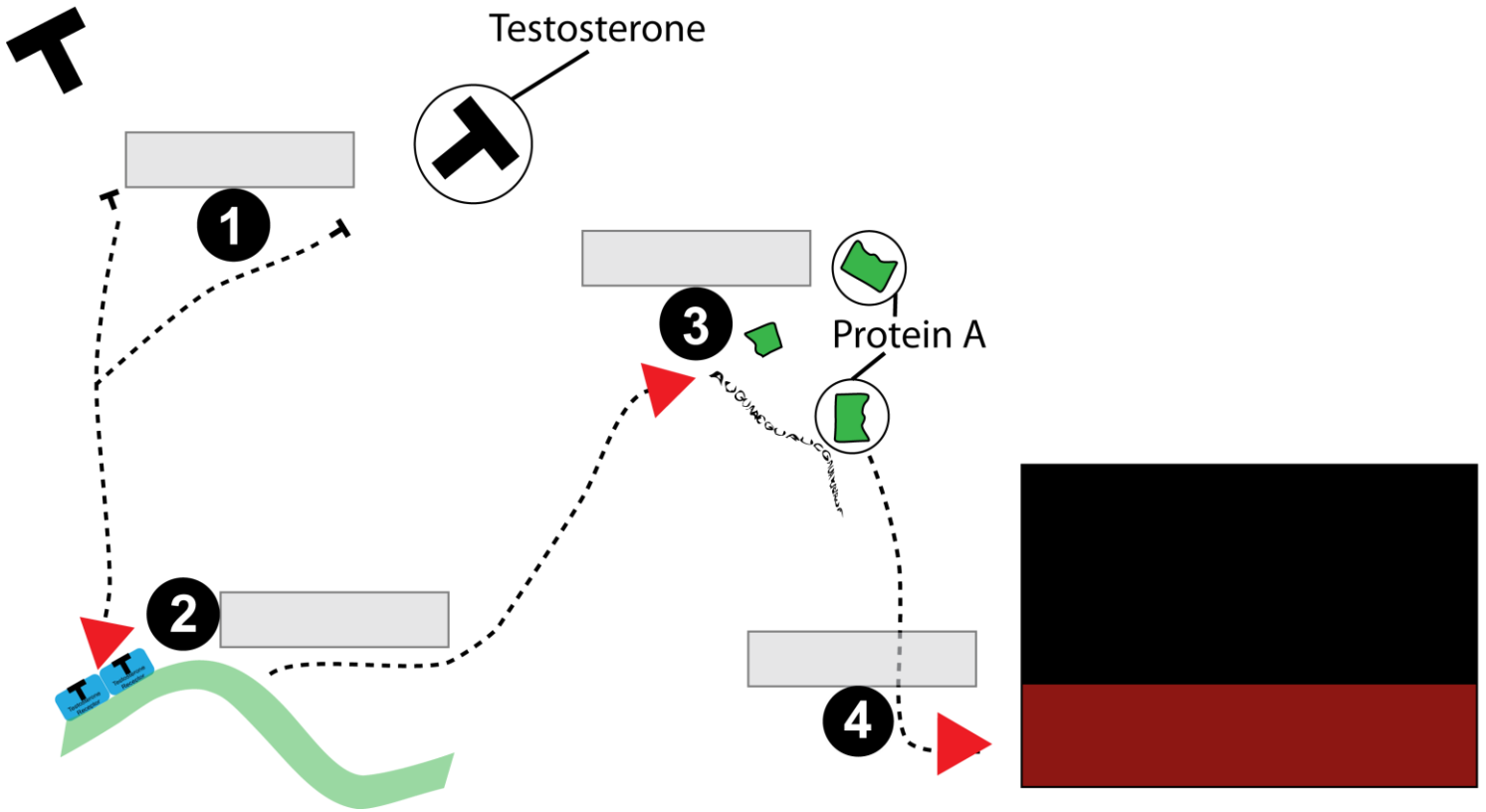
Male--Brain Map Overlay

For Part 3 (*print on transparency*)

Female--Brain Map Overlay

For Part 6 (print on transparency)

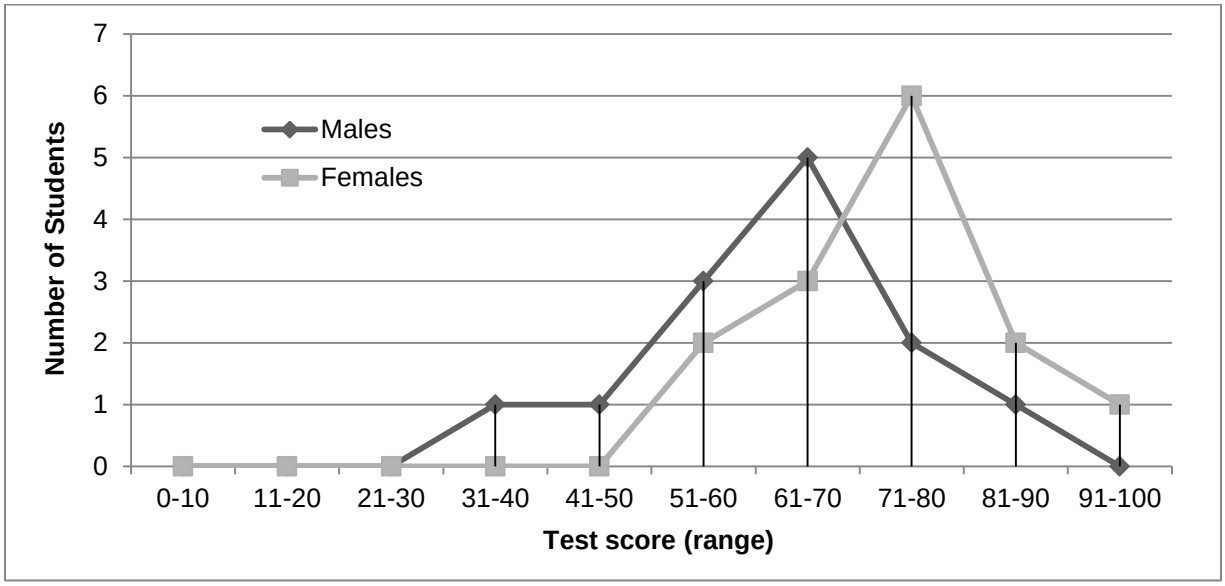
+ Testosterone Signaling



Part 1: Don't get testy!

Introduction:

Ms. Smith, the high school English Language Arts teacher, made a graph of the exam scores from a recent test she gave her 27 students as she always did. This time, however, she decided to plot the results for the 13 males and 14 females separately. While there was considerable overlap in performance between male and female students, on average there was a slight difference between the groups.



1. As a group, who performed better on the exam, males or females?

   Females

2. What is one possible reason that could explain the different performance of males and females on this English test?

   - ***Random chance due to small sample size (27 students)***
   - ***Different cognitive abilities between males and females***
   - ***Other social or environmental factors that could differently affect males and females***

3. Think of Ms. Smith's English test as an experiment.

   a. What is the independent variable? **The sex of the students**

   b. What is the dependent variable? **The test score**

Part 2: Do Male and Female Brains Work Differently?

Overview:

The following two neurological tests have been developed to test different types of memory. After taking one or both of the tests, compare the results for males and females in the class to determine if the results support the idea that male and female brains work differently.

Student Instructions

Memory Test #1 Instructions

1. Listen to the list of words read by your teacher.

2. Wait one minute after the last word is read.

3. Write as many of the words that you just heard as you remember in the table provided.

Scoring the test

4. After you finish writing the list of words, the teacher will read all of the words again. Place a mark next to all of the words that you remembered correctly.

5. Record your total # correct in the space provided.

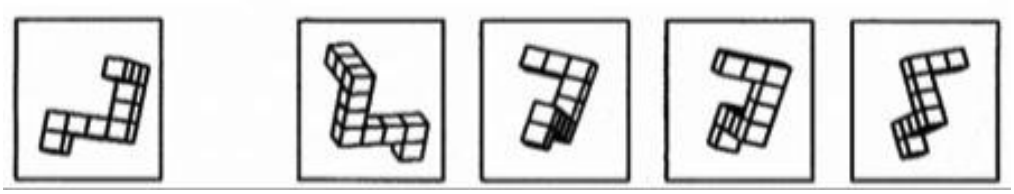
YOUR RESULTS	
Monday's Grocery List	Correct (√)
Your Total Number Correct	

Memory Test #2

1. The shape on the left is your model.

2. Of the 4 shapes on the right, 2 are the same as the model but have been rotated at a different angle.

3. Mark with an X below the 2 shapes that match the target. An example is given below.



X X

4. There are 8 total problems and you will have 4 minutes to complete them.

   Don't be upset if you don't finish as this is common.

<u>Scoring the test</u>

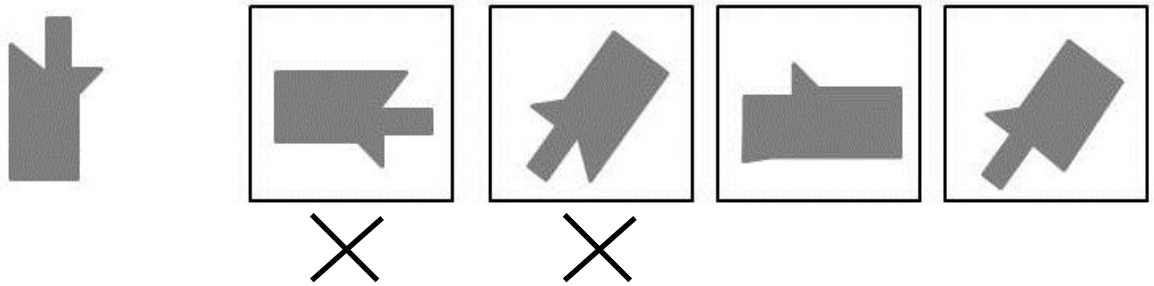
5. To score the test, you receive 1 point for each question in which you correctly identified BOTH of the matching models.

6. No points are awarded if one or more choices are incorrect.

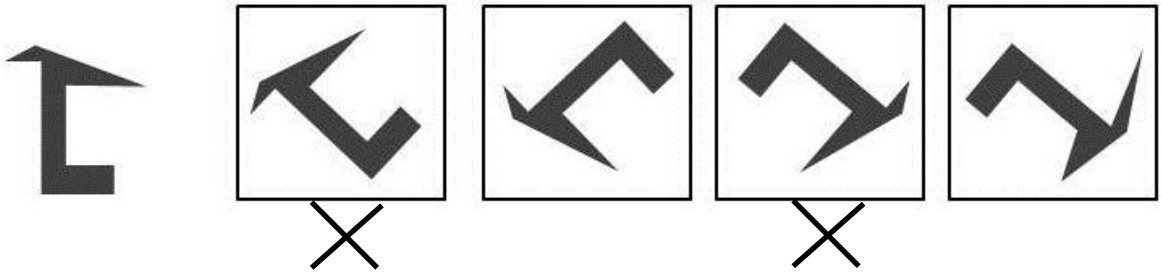
Mark with an X below the two figures on the right that match the one on the left.

There are 2 pages and 8 total questions.

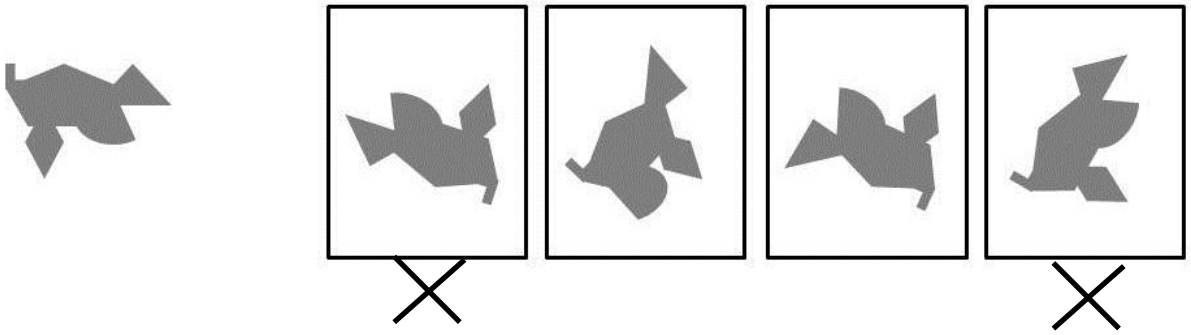
1.



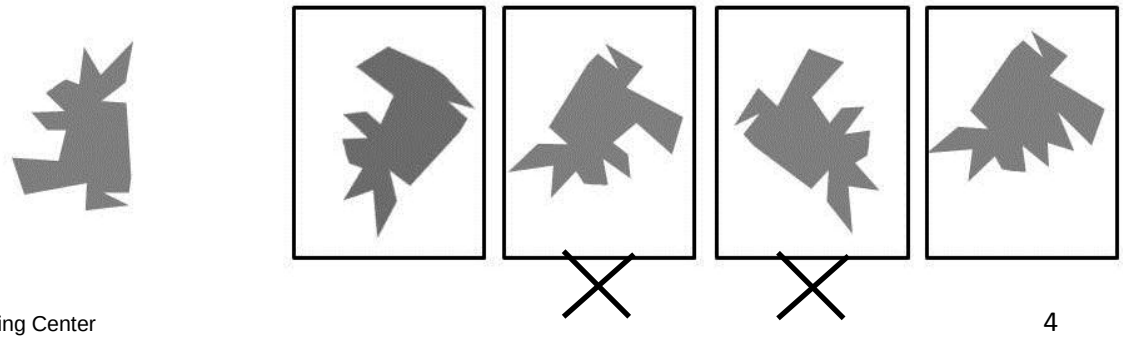
2.



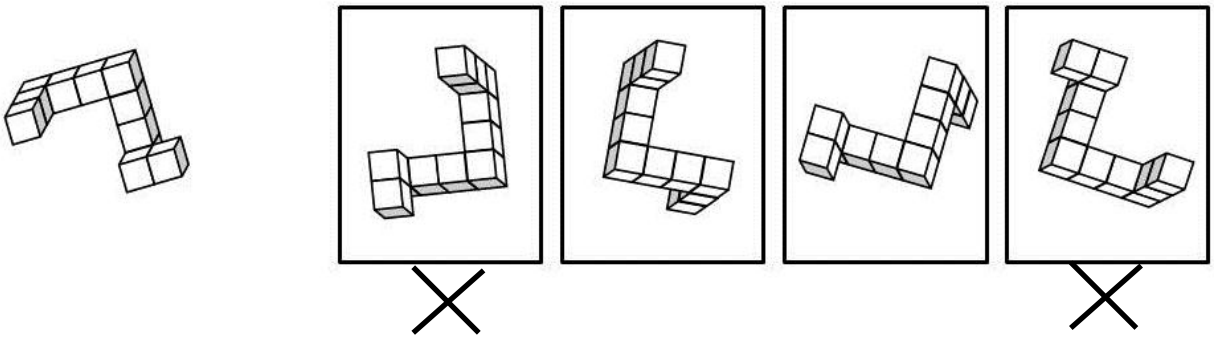
3.



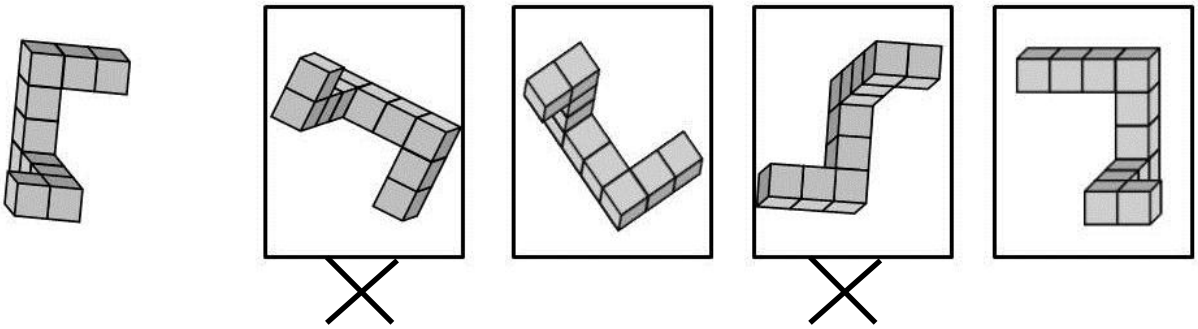
4.



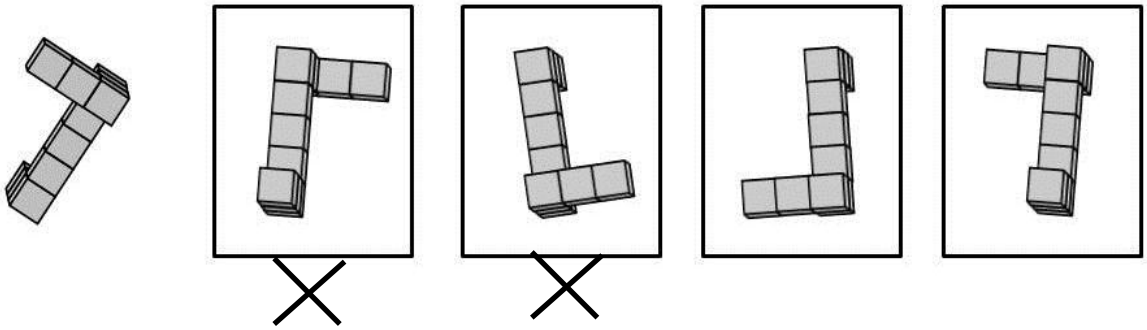
5.



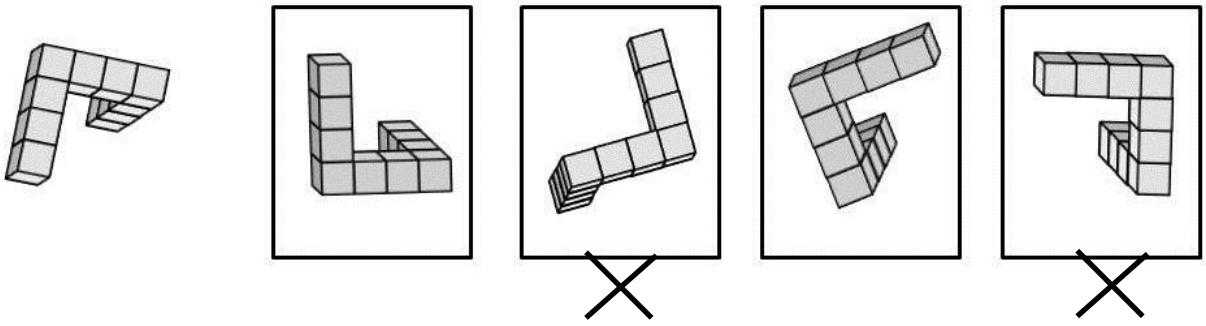
6.



7.



8.



Your Total Correct _____

VERBAL MEMORY--CLASS DATA		
	Total Correct	
Student #	Females	Males
1		
2		
3		
4		
5		
6		
7		
8		
9		
10		
11		
12		
13		
14		
15		
AVERAGE		

SPATIAL ROTATION TEST--CLASS DATA		
	Total Correct	
Student #	Females	Males
1		
2		
3		
4		
5		
6		
7		
8		
9		
10		
11		
12		
13		
14		
15		
AVERAGE		

Based on the class data, does it appear that males or females are better at either the verbal memory task or spatial rotation memory test?

***Answers will vary—opportunity to talk about sample size and the need for more careful analysis*.**

Teachers should emphasize that any differences observed between males and females on the two tests are most likely not enough to conclude that there are significant differences between the two groups. However, these tests when given to hundreds or thousands of males and females under controlled conditions (same lighting, same time of day) reveal average differences.

Part 3-Are There Physical Differences in Girls and Boys Brains?

There have been a number of studies comparing the size of brain regions in males and females. More work still needs to be done, but there appear to be some differences in the sizes of some brain regions between male and female brains. **THESE REPRESENT AVERAGES OF MANY MALE AND FEMALE BRIANS. INDIVIDUAL MALES AND FEMALES MAY BE MORE SIMILAR TO EACH OTHER.**

Examine the **Brain Map** and answer the questions below.

1. Which of the brain region(s) shown is/are involved in memory?

   Hippocampus, ***Cingulate Gyrus***

2. What is/are the function(s) of the amygdala?

   Basic Emotion

3. Place the **Male** and **Female Brain Map Overlays** over the **Brain Map** to identify regions of the brain where the average male and female brain may be different.

   - If the region appears only purple it indicates that region is similar in size between average male and female brains
   - **Where the pink overlay extends beyond the purple** indicates regions which tend to be **larger in female brains**
   - **Where the blue overlay extends beyond the purple** indicates regions which tend to be **larger in male brains**

Use the Brain Map and Male and Female Brain Map Overlay to complete the table below.

Brain Region	Function(s)	No difference or Larger in Males or Larger in Females
Amygdala	***Basic emotion***	***Larger in males***
Cingulate gyrus	***Emotion, learning and memory***	***Larger in females***
Hippocampus	***Learning and memory***	***Larger in females***
Hypothalamus	***Hunger, thirst, Sex***	***Larger in males***
Inferior temporal gyrus	***Form and color perception***	***Larger in males***
Lingual gyrus	***Vision and dreaming***	***Larger in females***
Prefrontal cortex	***Problem solving complex movements***	***No difference***
Thalamus	***Connection between brain regions***	***No difference***

Part 4-Neurological Disease in Males and Females

Biology Brief: Understanding Human Neurological Disease

Biology and math are combined in the field of epidemiology (EPPY-DEE-ME-AH-LO-GEE). Epidemiologists study disease rates among the population. These types of studies have revealed that there are some neurological diseases that are more common in males and others that are more common in females (**Table 1**).

Table 1: Percentage of Males and Females in U.S. Population with Neurological Conditions

Neurological Condition	Females	Males
Parkinson's—Loss of motor control	0.01%	0.02%
Multiple Sclerosis	0.1%	0.03%
Mood Disorders (Depression)	5.9%	3.9%
Tourette's Syndrome	0.08%	0.23%
Autism	0.2%	0.8%

Questions:

1. Which neurological conditions affect more males than females?

   Parkinson's, Autism, Tourette's

2. Which neurological conditions are more frequent in females?

   Multiple Sclerosis, Mood Disorders

3. Provide two possible explanations for the differences in neurological disease rates between males and females? Explanations can include information presented in this lesson or other sources.

   Differences in the brain/nervous system between males and females.

   Different hormones produced by males and females.

   Genes located on the X or Y chromosomes which differ between males and females

   Environmental factors like peer pressure may affect males and females differently

   Differences in the rates that males and females seek medical treatment. Maybe more males do suffer from depression but are undiagnosed because of unwillingness to seek help.

4. Provide an explanation for why there are no neurological diseases that affect only males or females?

   Male and female brains have much in common and individual males and females can be similar.

Part 5-Hormones and the Brain

Biology Brief: Sex Hormones and the Brain

Hormones, chemical messengers released by specialized organs called endocrine glands, can travel throughout the body through the circulatory system. Hormones affect the development and function of other organs including the brain. Humans have about 50 different hormones including some that are produced by the sex organs (testes and ovaries) called sex hormones.

Testosterone and estrogen are two sex hormones that play important roles during development from embryonic stages through puberty and into adulthood. These hormones are best known for inducing the formation of secondary sex characteristics but testosterone and estrogen can also affect brain development. The level of sex hormones changes throughout development and can affect brain cells in different ways including:

- **Promote cell division** (mitosis)
- **Increase cell growth** (change in cell size and shape)
- **Induce cell death** (apoptosis)
- **Increase cell communication** (nerve firing)
- **Direct cell differentiation** (development of specific types of neurons)

There are many different types of nerve cells in the brain (like cortex nerve cells, hippocampus nerve cells, amygdala nerve cells). Different nerve cells may respond in different ways to the same hormone.

Questions:

1. Hormones are released by _____***endocrine glands***_____.
2. Answer the true false questions below.

Sex hormone levels do not change throughout development	TRUE	**FALSE**
Sex hormones are active only during puberty	TRUE	**FALSE**
Sex hormones can affect cell division in the brain	**TRUE**	FALSE

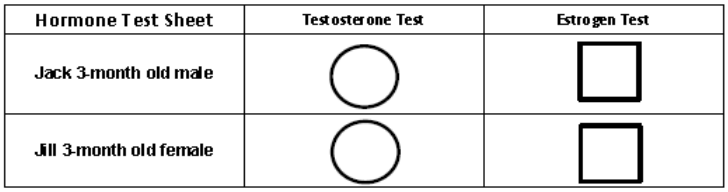
3. List three ways that sex hormones can affect neurons.
   - **Induce cell growth**
   - **Induce cell death**
   - **Promote cell division**
   - **Affect cell differentiation**
   - **Affect nerve cell firing/signaling**

Overview:

The hormones testosterone and estrogen can be detected in the blood plasma (liquid part of the blood). Your lab kit contains samples of blood plasma collected from Jack and Jill, 3-month old male and female fraternal twins. Your goal is to determine if there are any differences in testosterone or estrogen at this critical stage of brain development.

Follow these instructions to determine the levels of testosterone and estrogen in each of the blood plasma samples.

1. Place 1 drop of Jack's plasma sample in the top circle and the top square.



2. Using a clean dropper place 1 drop of Jill's plasma sample to the bottom circle and bottom square.

3. Using a clean dropper add 1 drop of Testosterone Test Solution to both of the circles. Use the COLOR CHART to record your results below.

4. Carefully place a piece of the Estrogen Test Paper onto both of the squares. Use the COLOR CHART to record your results below.

Patient	Testosterone Level (nanograms/100 ml)	Estrogen Level (nanograms/100 ml)
Jack, 3-month old male		
Jill, 3-month old female		

4. Based on the information in the data table:

- Which hormone (testosterone or estrogen) is most different between males and females at this stage?

Testosterone

- Are either testosterone or estrogen secreted in only males or only females?

No

Part 6-Sorting out the Signals

Biology Brief: The Steps of Hormone Signaling

Scientists are still trying to understand how exactly testosterone signaling can influence cells in the brain and perhaps lead to differences between male and female brains (**Figure 1**).

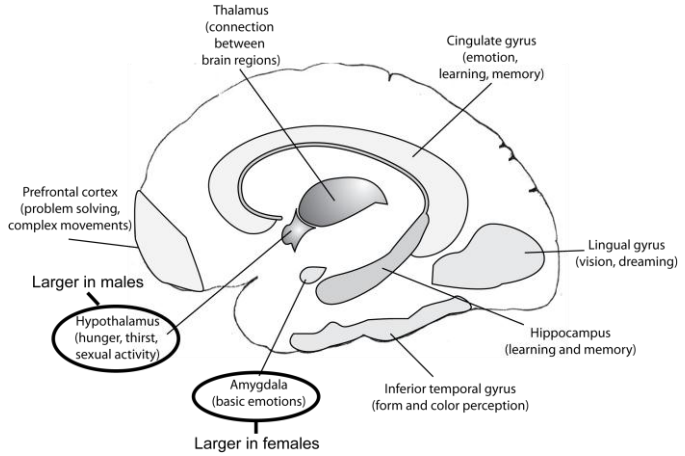


Figure 1: Testosterone signaling may contribute to differences between male and female brains.

Some of the major steps have been worked out. They include the following:

1. In the brain, testosterone can bind to proteins called testosterone receptors within neurons. Unlike many receptors, testosterone receptors are found in the cytoplasm not at the plasma membrane.
2. After binding to the testosterone, testosterone receptors enter the nucleus. In the nucleus, testosterone receptors bind to DNA and other specialized proteins to turn on or off transcription of other genes.
3. Genes activated by testosterone signaling are then translated into proteins in the cytoplasm by ribosomes.
4. Proteins turned on or off by testosterone signaling can then affect neuron functions such as:
    - **cell division** (mitosis)
    - **cell growth** (change in cell size and shape)
    - **cell death** (apoptosis)
    - **cell communication** (nerve firing)
    - **cell differentiation** (development of specific types of neurons)

The effects of testosterone can be different in different nerve cells because these cells may already have different proteins present before receiving the testosterone signal. These other proteins may then change how the cell responds to the testosterone signal.

Activity- Following the Signaling Steps

Overview: The goal of this activity is to help demonstrate how testosterone can affect different neurons in different ways. This may help explain the average differences in size observed between males and females in certain brain regions like the hippocampus and the amygdala.

Instructions:

- Obtain the following supplies from your teacher
  - **Hippocampus Neuron** sheet
  - **Amygdala Neuron** sheet
  - **Testosterone Signaling Pathway** overlay
- With the **Hippocampus Neuron and Amygdala neuron** models in front of you determine if the following cell parts are present and where they are located within the cells.

	Hippocampus Neuron		**Amygdala Neuron**	
Cell Part	**Present** (√)	**Location** (plasma membrane, cytoplasm or nucleus)	**Present** (√)	**Location** (plasma membrane, cytoplasm or nucleus)
Gene A (encodes Protein A)				
Testosterone Receptor				
Protein B				
Ribosome				

Questions:

1. What cell part(s) is/are present in both the Hippocampus and Amygdala neurons?

Gene A, Testosterone Receptor, Ribosome, RNA Polymerase

2. What cell part(s) is/are missing between the Hippocampus and Amygdala neurons?

Protein B

Instructions (continued)

- Model the effect of hormone signaling by positioning the **Testosterone Signaling Pathway Overlay** onto the **Hippocampus Neuron** so that the testosterone molecules (resembling a T) are fit into the Testosterone Receptors.
- Cut out the **Signaling Step Tags** below (BOTTTOM RIGHT) and place them in the spaces near the numbers on the **Testosterone Signaling Pathway Overlay** to identify what is happening at each step.
- Complete the table below when you are finished.

Step	Label used
1	Receptor Binding
2	Transcription
3	Translation
4	Cell Effect

Questions:

3. What may happen to the Hippocampus Neuron in response to testosterone signaling?
   (Hint: refer to step 4)
   The cell may die

Note that we can only what MAY happen to the cell because the result will depend on the exact timing and amount of testosterone signal received by the neuron.

Instructions (continued)

- Repeat this process with the **Amygdala Neuron** model and the testosterone.
- Answer the questions below using the model and the information in **Part 6-- Biology Brief: The Steps of Hormone Signaling**

Questions

1. Describe what happens in Step 2 of the model?
   In the nucleus, testosterone receptors pair with other testosterone receptors and bind to DNA to turn on transcription of another gene.
2. What may happen to the amygdala neuron exposed to testosterone?
   The cell may grow

Signaling Step Tags
cut along dotted lines

Translation

Receptor Binding

Transcription

Cell Effect

Extension Questions

3. How might testosterone's effects on these nerve cells contribute to the average differences between male and female brains presented in PART 2?

   The amygdala is larger in males—maybe due to testosterone promoting growth

   The hippocampus is smaller in males. This might be due to cells dying in this part of the male brain.

4. Given what we know about the brain and male and female differences do you think that male and female students should be treated differently? Graded separately?

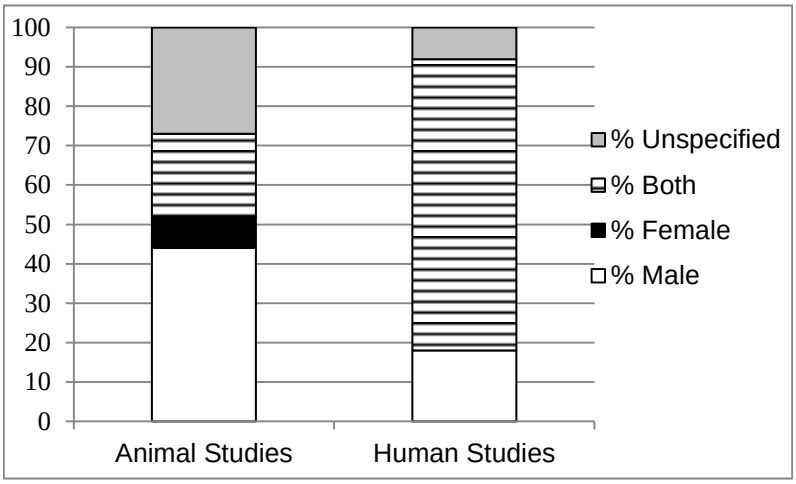
   Answers will vary. Students in favor of different treatment should cite the differences observed in the brain regions associated with learning, memory, and vision. They may also note any differences between the males and females of the class performance on the memory tests.

   Students in favor of equal treatment should include the fact that there is great overlap between males and females in tests of knowledge and memory. Also they may note similarity between male and female brain anatomy in the prefrontal cortex

Part 7: Bias-ology

Animal models, like mice and rats, are one of the most critical ways that scientists can understand the causes and potential cures of human diseases. Though there are clearly diseases that are more common in females than males, most animal research is performed with male animals. A recent examination of published biological research revealed that in the field of neuroscience males were used 5 times more often than females in single sex animal studies.

Figure 1: Percentage of male and female animals included in published neuroscience research papers in 2009.



(Beery and Zucker, 2010, Neroscience Behavior Research)

Some scientists say using males is less expensive and easier than using female animals. For one, the hormonal cycle of female animals requires that hormone levels be measured and matched among experimental groups. This requires more time, animals, and money, which researchers argue is in short supply.

Others believe that animal studies must include male and female animals and compare them separately to determine if there are differences between the sexes. One possible negative consequence of not studying females is that new drugs that work in males may have unanticipated side effects in females. Supporters of female research also argue that studying females may benefit both males and females. In one case, researchers found that pregnancy decreased symptoms of multiple sclerosis in female mice. This has led to studies exploring whether female sex hormones can help treat this disease in males.

1. Approximately what percentage of non-human animal studies included females? **~30% (%female + %both)**

2. What are the arguments against using female animals to study disease?

   Higher cost, More animals used. More difficult to control for hormonal differences between individuals

3. What are the arguments for using females in animal research studies?

   Better understanding of the causes of disease in females. Development of treatments for females and males.