Enhancing the Physiological Psychology Course through the Development of Neuroanatomy Laboratory Experiences and Integrative Exercises

Steven A. Lloyd
North Georgia College & State University

Author contact information:
Steven A. Lloyd, Ph.D.
Assistant Professor of Psychology
North Georgia College and State University
Department of Psychology
Dahlonega, GA 30597
(706) 864-1445
salloyd@ngcsu.edu

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Introduction:

This resource is a guide designed to supplement a typical upper level Physiological Psychology or Behavioral Neuroscience course or to serve as a stand-alone, expandable laboratory experience. The guide includes 10 assignments, answer keys, and references that reinforce and expand upon students' learning and stimulate interesting class discussions. See Table 1 (next page) for a list of the assignments and how they coincide with chapters in Carlson's (2007) text. The first assignment is also based on Vanderwolf and Cooley's (1979) sheep brain atlas. The assignments can be easily adapted for use with other physiological psychology texts or assigned in different orders because they do not depend on each other. The Table of Contents notes specific pages for the start of each segment of the guide. Additional front matter gives advice for the novice instructor on how to design and conduct a neuroanatomy laboratory using biological tissue.

Texts

Carlson, N. R. (2007). *Physiology of behavior* (9th ed.). Boston: Allyn and Bacon.

Vanderwolf, C. H., & Cooley, K. C. (1979). *The sheep brain: A photographic series* (2nd ed.). London: A. J. Kirby.

Overview of Assignments

1. Sheep Brain Dissection Guide: This guide not only steps the students through dissection procedures for identification of major central nervous system (CNS) structures, regions, and systems from both a gross and microscopic perspective, but it also contains a set of questions meant to guide students toward a deeper understanding of structure-function relationships. It also serves to introduce students to material and systems that are normally discussed throughout the semester. The student guide and associated questions are listed first to facilitate distribution to students. This is followed by a second copy of the guide and questions, with suggested answers embedded after each question. All of the answers have been italicized for emphasis. Page numbers with each segment of the guide reference Vanderwolf and Cooley's (1979) sheep brain atlas.

2. – 10. Paper Prompts: Each of these assignments is a half-page or less prompt suitable for stimulating short (1-2 page) individual student papers and class discussion. Some of the assignments contain additional references or instruct students to find academic sources. Each assignment is followed by an answer key or description of points students will probably make in their responses.

Acknowledgements

I would like to thank Dr. Ruth Ault for her numerous editorial contributions in the development of this resource.

Table 1
Correspondence Between Assignments and Carlson Text Chapters

Assignment	Carlson (2007) Chapter Numbers
1. Sheep Brain Dissection	2 and 3
2. Neurotoxins	2 and 4
3. Neurophysiology	2 and 4
4. Prosopagnosia	6 and 7
5. Mirror Neurons	8, 11, and 13
6. Cranial Nerve Zero	10
7. Sexual Orientation	10
8. Hypothalamic Neurogenesis	10, 12, and 13
9. Addiction	13 and 18
10. Movement Disorders	15

Table of Contents

I. Designing a Neuroanatomy Laboratory

A. How to Set Up Your Neuroanatomy Laboratory Experience

Below is a list of the scientific supply companies referenced in this manual. Many others exist. To order materials from these companies, you may need to establish an institutional or personal account and provide them with shipping and purchasing information. Most companies will require a purchase order or credit card number before they will ship the items. Each company has its own procedures, so you should contact them directly to determine how to comply. Alternatively, your Materials Management or Purchasing departments may do this for you.

Each company's website can provide additional information concerning the items to be purchased as well as their retail prices. Many companies provide discounted rates for educational purchases and for state institutions (e.g., tax and shipping exemptions). You might also wish to contact your sales representative for that supplier to receive a quote on the items you wish to order. Your representative may be able to provide additional discounts. Make sure to ask for estimated shipping charges, which may not be calculated ahead of time, but which may produce unexpected expenses. Additional hazardous shipping rates may apply for some materials (especially for biological specimens and chemicals). Check with the manufacturer before ordering.

COMPANY	PHONE	FAX	ADDRESS	WEB ADDRESS
Fisher Scientific	1(800) 766-7000	1(800) 926-1166	81 Wyman Street Waltham, MA 02454	www.fishersci.com
Electron Microscopy Sciences	1(800) 523-5874	(215) 646-8931	321 Morris Rd. Box 251 Fort Washington, PA 19034	www.emsdiasum.com
Carolina Biological Supply Co.	1(800) 334-5551	1(800) 222-7112	2700 York Road Burlington, NC 27215	www.carosci.com
VWR International	1(800) 932-5000		1310 Goshen Parkway West Chester, PA 19380	www.vwr.com
Blue Spruce Biological Supply, Inc.	1(800) 825-8522	(303) 688-3428	701 Park St. Castle Rock, CO 80104	www.bluebio.com

Below is a short list of items to support a neuroanatomy laboratory experience. Although all items are included for thoroughness, the list can be pared down based on your specific laboratory goals.

PRODUCT	PRODUCT DESCRIPTION	COMPANY	ORDER No.
Brains	Sheep Brain w/ Hypophysis	Fisher	S9226S
Brains	Sheep Brain Student Grade	Fisher	S92265
Spinal Cord	4" Cow Spinal Cord Portion	Carolina	228920
Spinal Cord	4" Cow Spinal Cord Portion	Fisher	S1711S
Eyes	Sheep Eyes (package/10)	Fisher	S9224S
Histology Slides	Cerebellum	Blue Spruce	HE1-32
Histology Slides	Cerebral Cortex	Blue Spruce	HE1-21
Histology Slides	Spinal Cord cross section	Blue Spruce	HE2-22
Histology Slides	Peripheral Nerve	Blue Spruce	HE3-11
Histology Slides	Motor Nerve Cell	Blue Spruce	HE4-1
Histology Slides	Hypophysis	Blue Spruce	H01-1
Histology Slides	Sensory Organ Detail Set (10 slides)	Fisher	S64950
Histology Slides	Nervous System Detail Set (11 slides)	Fisher	S64949
Preservative	Biofresh Concentrate	Fisher	S6011S
Containers	6 Gallon Pail with Lid	Fisher	S6020
Containers	12qt Buckets	Fisher	S30518A
Dissection Knife	190mm Disposable Autopsy Knife	EMS	63010-01
Scissors	Student Scissors	Fisher	S17310
Trays	Dissecting Pans with Wax	Fisher	09-002-20
Gloves	Fisherbrand Nitrile Gloves (M & L)	Fisher	19-050-221
Dissecting Needles	Dissecting Needles (package/12)	VWR	257778-000
Dissecting Needle	Dissecting Needles (package/12)	Fisher	08-965A
Dissecting Kit	Individual Student Dissecting Kit	Fisher	S17259
Sheep Brain Atlas	The Sheep Brain: A Photographic Series	Amazon.com	920700039

B. Important Practical Considerations in Developing a Neuroanatomy Laboratory

All biological specimens are packaged with a preservative and should also be stored in a preservative between uses (e.g., Fisher packages some materials in a non-formaldehyde containing preservative called BioFresh, which can be purchased separately for specimen storage). Precautions should be taken in handling these materials. You should follow your institution's chemical safety regulations regarding the handling, use and disposal of these materials. Additional information can be obtained from the manufacturer in the form of Material Safety Data Sheets (MSDS). MSDSs provide a wealth of information including chemical content information, health risks, emergency procedures, first aid measures, fire fighting measures, accidental release measures, storage and handling information, etc.

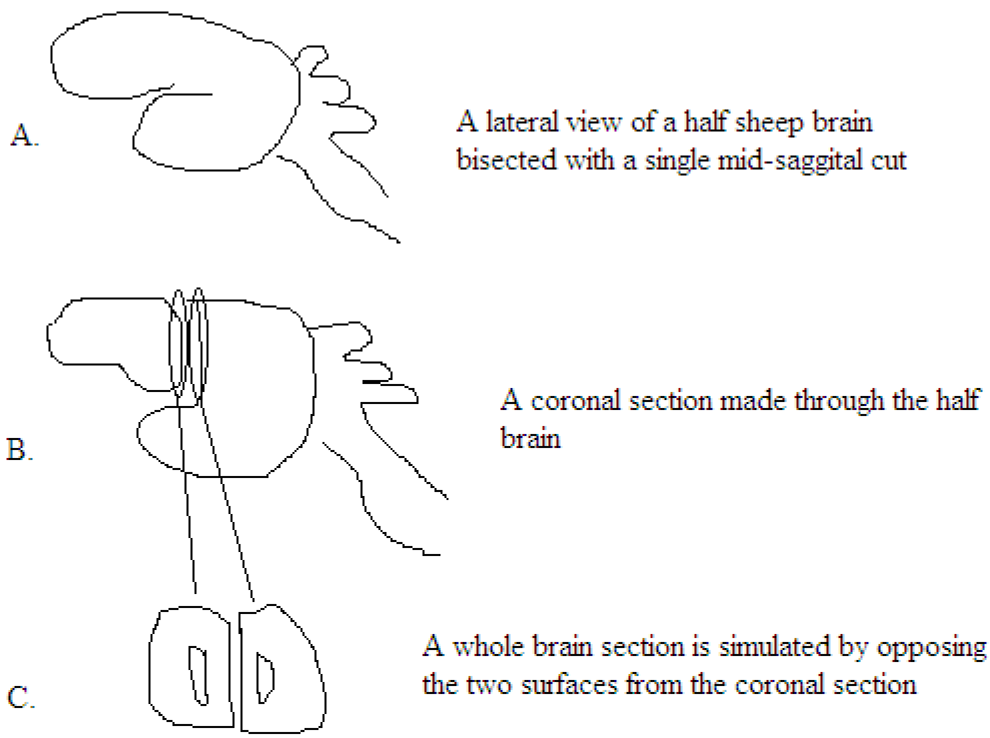
You should provide gloves for handling the biological specimens. To avoid issues with possible latex allergies, you may wish to use latex-free gloves. There are many latex-free alternatives on the market (e.g., Nitrile brand gloves). Depending on how the specimens have been preserved and stored, you may also wish to provide surgical masks. Alternatively, instruct students to place the specimen under running water before performing laboratory sessions to help remove excess chemicals and reduce vapors.

Scissors and dissecting knives can be shared, but students should have their own dissecting needle(s) and atlas and each group should have its own trays. Order enough buckets and preservative for short-term and long-term storage. Buy some cheap rags and string. Once the students start sectioning their brains, the string can be used to keep each brain together and separate from other students' in between lab sessions. Instruct the students to avoid letting the specimens dry out during the laboratory sessions. They can use the rags mentioned above dipped in the preservative to moisten the specimens and to cover those not being used. This should be done frequently during each laboratory session.

Most students will benefit from a small group experience during the brain anatomy laboratories. This is also a cost efficient strategy. It is my observation that group size should be limited to two or three students per group. Large groups may reduce the level of involvement for some group members. Be sure to instruct students that all members of the group must "get their hands wet."

Although many of these items will need to be purchased by the institution, some may be a required purchase for the student (e.g., Sheep Brain, Spinal Cords, Sheep Eyes, and Student Dissecting Kits). This can be arranged by contacting your bookstore manager. Many bookstores are experienced at ordering these types of materials for students in Natural Sciences courses.

Each group will be working with one brain for whole brain inspection as well as for midsagittal and several coronal sections. Allow the students to observe all visible whole brain structures before making the midsagittal cut (i.e., dividing the two hemispheres). Instruct the students to keep one half of the brain intact for reviewing midsagittal and whole brain structures and to work exclusively with the other half for the remaining coronal sections. Perform the coronal sections in the order suggested using the landmarks highlighted in the lab book (Vanderwolf & Cooley, 1979) for this half brain. After making each successive coronal section, use that section and the remaining intact half brain to simulate a whole brain section (see figure below).



C. Useful Web Links for Students and Faculty

A few of the many excellent web-based resources in neuroanatomy are listed below. If you are considering developing a neuroanatomy lab, but are limited in resources, you might consider utilizing some of these materials as a substitute for real tissue.

1. http://www.gwc.maricopa.edu/class/bio201/brain/1neuro.htm
This website contains several pictures of sheep brain sections, including "hard to get to areas." Students can also test their knowledge of 30 midsagittal structures by completing an on-line quiz.

2. http://www.exploratorium.edu/memory/braindissection/
This site is dedicated to the anatomy of memory. It includes a video of a sheep brain dissection.

3. http://academic.scranton.edu/department/psych/sheep/
This excellent sheep brain dissection resource is currently under development. Several of the concepts listed in this guide are reinforced. Check back regularly for regular additions to the site.

4. http://www.wellesley.edu/Biology/Concepts/Html/sheepbrain.html
The site includes a digital video of a dissection of the hippocampus from a whole sheep brain (a hard to reach brain region).

II. Assignments and Answer Keys

A. Assignment 1: Sheep Brain Dissection Guide and Associated Questions

Use this guide along with your lab book (Vanderwolf & Cooley, 1979) to help you locate structures in the brain, identify the functions of these structures, and identify major functional brain circuits. Answer all of the questions in this lab manual and turn them in as Assignment #1.

I. Meninges

1. The brain has a three-layered covering collectively called the meninges.
    a. What are the names of each layer starting with the inner most layer and moving out?
    b. Name three major functions of the meninges.
2. Before you remove the meninges, note the cranial nerves emerging mostly from the base of the brain (see V & C, p. 18).
3. Remove the meninges from your sheep brain using scissors and forceps. Be careful not to remove the pituitary gland. Also be very careful in removing the tentorium (the dura that separates the cerebellum and cerebral cortex). Note the thickness and toughness of the two outer layers of the meninges and the fragility of the third layer (which is probably still attached to the brain). Notice how the third layer dips into the sulci, following the contours of the brain.
    a. Which layers compose the tough stuff?
    b. Which layer is delicate and most closely associated with the brain's surface structures?
4. Delicately remove the final layer of the meninges, being careful not to disrupt the cranial nerves on the ventral aspect of the brain.
    a. Which aspect is ventral? Which aspect is dorsal?
    b. Rostral? Caudal? Anterior? Posterior?

II. Surface Features of the Brain (V & C, p. 16-17)

1. Attempt to locate the lobes of the brain and review the human counterparts and functions.
    a. What will you use as your landmarks? How do they differ from the human brain?
    b. Name a primary cortical area contained in each of the four lobes of the human brain.
2. What is the difference between a sulcus and a fissure? A sulcus and a gyrus?
3. In the human brain, what is the name of the gyrus that contains the primary motor cortex? The primary somatosensory cortex?
4. Gently lift and pull the cerebellum caudally, being careful not to pull too hard, and gently pull the cerebral cortex rostral. Observe the corpora quadragemina.
    a. What structures compose the corpora quadragemina?
    b. What's another name for these structures?
    c. What lies immediately ventral to these structures?
    d. What is the function of these structures?

III. Ventral View (V & C, p. 18)

1. Identify as many of the cranial nerves as you can see (note: the cranial nerves are delicate and many will not survive your dissection of the meninges).
    a. What do they do (generally)?
    b. Name each of the 12 cranial nerves in order starting with cranial nerve I.
2. Mammillary Body (MB)
    a. What is it connected to?
    b. Why might Korsakoff's syndrome, which targets the mammillary bodies, result in anterograde amnesia?
3. Infundibulum
    a. It connects _____ to _____.
    b. What is so important about this connection?
4. Optic Tract/Chiasm – this is where part of the visual world decussates (see V & C, pp. 89; 101-103 for additional help).
    a. What does decussate mean?
    b. Which parts of the eye decussate?
    c. How does the fact that some processes decussate and others do not determine the location of the left vs. the right visual fields?
5. Olfactory system (refer to V & C, p. 93 for additional help)
    a. Where are these sensory projections sent in the brain?
    b. What is the first major stop of other sensory projections in the brain (Hint: it is part of the diencephalon)?
    c. What are some of the implications for the unique projection pattern for olfactory sensory fibers?
6. Temporal Lobe
    a. Name two limbic structures that are located deep within the temporal lobe.

IV. Midsagittal View (V & C, pp. 21-22)

1. Spinal Cord, Medulla, and Pons
    a. These are contiguous structures. How are they similar? How are they different?
    b. What developmental division of the brain do these structures develop from?
2. Midbrain
    a. What are the six major nuclei that make up the midbrain?
    b. What are the major functions of these nuclei?
    c. In general, what is the overall function of the midbrain?
3. Diencephalon
    a. The diencephalon is made up of which two major structures?
    b. The name of one of these diencephalon structures suggests its anatomical position in relation to the other. Which structure? What direction is provided by the name?
    c. What are the major functions of each of the two structures of the diencephalon?
4. Cerebral Cortex - make sure you can locate the different lobes and surface features of the human brain from pictures in your textbook. Try to locate analogous regions in the sheep brain (see V & C, p. 81 for additional help).
    a. What primary sensory cortical area is located in the temporal lobe?
    b. Which lobe is anterior to the parietal lobe? What primary cortex is contained in this lobe and, therefore, what are some of the major functions of this area?

c. Which lobe contains the primary visual area? What are the functional consequences of damage to the primary visual area compared to the visual association areas?

5. Cerebellum
    a. What happens to an animal when you damage its cerebellum, and what does this suggest about one of the major functions of the cerebellum?
    b. Cerebellum means small brain – look at its organization and suggest why.
6. The Ventricular System
    a. Identify and name the different ventricles, the regions of the brain they serve and related components. Describe how the different ventricles are interconnected to allow a flow of cerebrospinal fluid (CSF). Be sure to include the following terms in your answer: the Lateral, 3rd, and 4th ventricles; the septum pellucidum; the interventricular foramen; and the cerebral aqueduct.
    b. What is so important about the ventricular system and the CSF that it contains?
    c. Where is the CSF made?
7. Cingulate Gyrus
    a. I am calling your ATTENTION to this structure – Why?
    b. Which brain system does the Cingulate Gyrus belong to?
    c. What does this suggest about another of its functions?
8. Corpus Callosum (CC)
    a. It is a commissural system – what does this mean and what does it connect?
    b. Name the other commissural systems.
9. Massa intermedia - what does it connect?
10. Hippocampal formation (if you can see it): Hippocampus means sea horse.
    a. What happened to HM when he lost this structure?
    b. What does the loss suggest about the function of the hippocampus?
11. Tectum (roof)
    a. What two structures compose the tectum?
    b. Which sensory systems project to which colliculi?
    c. Without looking in your book, which colliculus is closer to the dorsal aspect of the brain, the superior or inferior? Explain how you came to your answer.
12. Tegmentum (floor)
    a. Name several nuclei contained in the tegmentum.
    b. Two of the nuclei in the tegmentum are dopaminergic. Name the nuclei and explain what dopaminergic means.
    c. Which dopaminergic nucleus in the tegmentum degenerates in Parkinson’s disease, and which one is involved in drug addiction?
    d. Which nucleus is involved in pain perception?
13. Anterior Commissure (AC) and Posterior Commissure (PC)
    a. What good are they?
14. Pineal gland
    a. What is its historical significance?
    b. What is it now known to do?

V. Special Dissections (V & C, pp. 23-26)

Do not try to replicate these dissections, but use the pictures to help understand the 3-D organization of the brain and the following structure-function relationships:

1. Visualize how information from the optic tract flows first to the relay nucleus (thalamus) and specifically to the lateral geniculate nucleus.
    a. Why is it called the geniculate nucleus? What does it look like?
    b. These fibers are relayed to three major regions of the brain. Indicate what the information might be used for within these structures:
        i. Suprachiasmatic nucleus of the hypothalamus
        ii. The Superior Colliculus
        iii. The Occipital Lobe
    c. What is the thalamic division that relays auditory information?
    d. Name the main destination for auditory information after the leaving the thalamus.
2. Notice the internal capsule which contains fibers coming to the brain and fibers going from the brain. These fibers all converge near the thalamus. Because these projection fibers splay out (diverge) into cortical regions, they are called the optic radiations.

VI. Cross Sections (refer to V & C, p. 28, for help in determining where to section)

1. Coronal section through the optic chiasm (Section E in V & C, on p. 33)
    a. Gray matter and white matter
        i. What makes matter gray versus white?
        ii. What cell type makes the white stuff?
        iii. What is the physiological significance of the white stuff?
    b. The Striatum
        i. Which two nuclei make up the striatum?
    c. Globus pallidus along with the striatum forms the basal ganglia (BG).
        i. What is the general function of this brain circuit?
        ii. Name two neurodegenerative disorders that target this brain circuit.
    d. Internal/External/Extreme Capsule and corona radiata are all fiber pathways sending information to and from the cerebral cortex.
    e. Corpus callosum
        i. What does corpus callosum mean?
        ii. What is the structure immediately ventral to the corpus callosum?

2. Coronal section through the mammillary body (Section G in V & C, p. 35)
    a. Thalamus
        i. Attempt to locate the different divisions of the thalamus discussed at IV. 3.
    b. Hippocampal formation
        i. What is the general function of the hippocampus?
        ii. What does hippocampus mean?
    c. Amygdala (means almond)- it’s all the RAGE
        i. What might happen if you lesion someone’s amygdala?
    d. Lateral Ventricle
        i. What number ventricle is this?
    e. Limbic or Cingulate Cortex (located superior to the cingulum and corpus callosum)
        i. Name at least one function associated with this structure.

3. Coronal section through the cerebral peduncle (Section H in V & C, p. 36)
    a. Hippocampus & dentate gyrus
    b. Lateral geniculate nucleus (part of the thalamus)
    c. Substantia nigra
        i. What neurotransmitter is used by this nucleus?
        ii. What neurodegenerative disorder targets this structure?
        iii. What forebrain nuclei does this target project to?
        iv. What is the function of this nucleus?
    d. Superior Colliculus

VII. Horizontal Brain Sections (refer to V & C, pp. 29-30):
Horizontal sections demonstrate the three dimensionality of the brain, providing an overview of the location of most structures in relation to one another.

VIII. Spinal Cord Sections
Use V & C (p.105), text book, and lecture notes to help you locate the following portions of the spinal cord:

1. Gray matter, white matter, and central canal
    a. How is the organization different from the brain's organization?
    b. What is in the central canal?
    c. What brain system is the central canal continuous with?
2. Dorsal horn versus ventral horn
    a. Which way is dorsal and which way is ventral in the spinal cord?
    b. Why is this different from the orientation of the brain?
    c. Which horn contains the cell bodies of the motoneurons?
    d. What type of neuron is a motoneuron (i.e., describe its morphology)?
    e. Where are the cell bodies of the sensory neurons?
    f. What type of neurons are these sensory neurons (describe their morphology)?
3. Dorsal root versus ventral root (One of each serves the same basic region of the body and enters/exits the same area of the spinal cord; they are called spinal nerves).
    a. What type of fibers make up the dorsal root (sensory/motor)?
    b. What type of fibers make up the ventral root (sensory/motor)?
4. Spinal Nerve (see 3. above). Describe the organization of the spinal cord into functional segments or spinal nerves. How many spinal nerves are there and how are they grouped?
    a. Would there be a greater deficit after cervical or lumbar spinal cord damage?
    b. Why?
5. Dorsal Root Ganglion (DRG)
    a. What's in the DRG?
    b. Why are there no ventral root ganglia?

Microscopic Anatomy (Histology of Sensory and CNS Tissue)
Make sure to handle these <u>glass</u> microscope slides very carefully – they will break if you mishandle them.

I. Spinal Cord Sections (V & C, pp. 50-55):

Slide 70812e (Spinal Cord, Human – for general structure)
Slide Ma527e (Spinal Cord of Cat – stained for Nissl bodies)
Slide HE2-22 (Spinal Cord of Cat – Dorsal Root Ganglion Section)
Slide 70825f (Spinal Cord of Cat = light blue stain)

1. Locate the ventral horn of the spinal cord by first finding the motoneurons. Note: Depending on the tissue preparation that you have, you may only be able to see the soma and short stubs of the multiple processes. This will cause them to appear star shaped. They are clearly confined to one horn of the spinal cord – the ventral horn. Although you may see some nuclear staining in the dorsal horn, these cells are not as large and not multipolar in shape. Once you have found the motoneurons, move to the 10x objective for a closer look.
    a. What shape do they have?
    b. How are they different from the sensory neurons in the DRG?
2. Can you see the divisions of the white matter? What is the functional significance of these divisions? Note: Position the slide so that you are viewing the border of the spinal cord. The columns/fascicules should appear as delicate partitions. In fact they have small membranes that separate them from other surrounding columns/fascicules, almost like the sections of an orange (refer to V & C, pp.71-73; 77 for additional help).

Make sure you can identify the following structures in these histological preparations:

a. Gray matter and white matter

b. Ventral and dorsal horn: Note: The horns contain myelinated fibers (on the inside) and are the white matter with gray matter surrounding.

c. Dorsal root ganglion in some slides: Note: Position the slide so you are viewing outside of the spinal cord. The dorsal root ganglia may appear as a separate, round tissue structure with many stained nuclei. The DRG contain sensory neurons.

d. Motoneurons

e. Central Canal: Note: The central canal is in the very center of the spinal cord and is absent any staining, save the dark staining of the ependymal cells (specialized glia) that line the canal and, occasionally, also the choroid plexus (specialized glia that produce CSF).

II. Nerves (V & C, pp. 56-57)

Slide 70818e (Nerve, Human – cross section)
Slide HE3-11 (Nerve, Peripheral – cross section)
Slide 70817e (Nerve, Human – transverse section)

1. What is the definition of a nerve?

Note just how many fibers are contained within a given nerve segment. Many of these axons are myelinated. The myelin is only faintly stained, but the axon is darkly stained and located in the center. Note the segmentation of this tissue and the connective tissue that separates various segments. Some blood vessels can be seen as they course through the connective tissue.

2. The transverse section shows the length of the individual axons. You can still see the myelin sheath around the axon. Under high magnification, notice how the myelin is absent around very small regions of the axon. These are the Nodes of Ranvier.

a. What occurs at these Nodes?
b. What is the purpose of the myelin sheath?
c. Which cells make the myelin in the CNS? In the PNS?
d. If myelination is so beneficial, how come all axons are not myelinated?
e. What are some types of fibers that are likely to be myelinated? That is, what type of neural signals would likely need a fast reaction?

Make sure you can identify the following objects in these histological preparations:
a. Axons
b. Myelin sheaths
c. Nodes of Ranvier: Note: To see the Nodes, look in the transverse section and use high magnification (greater than a 10x objective may be necessary). You are looking for a thinning and then absence of the myelin sheath around the axon. Spend some time looking for it; it is worth the search.

III. Cerebellum (V & C, p. 60-61)
Slide 70803e (Cerebellum, Human)
Slide HE1-32 (Cerebellum, Human)

1. Observe the difference between the cerebral cortex (V & C, p. 58) and the cerebellum. Notice that each structure is made up of diverse cell types organized into layers. Using your text, describe how the cerebellum modulates movements based on the sensory signals received. Which part of the cerebellum receives the sensory signals? How do these sensory signals influence the output of the cerebellum? What is the result of the cerebellar output on the motor cortices?
2. Observe the three different layers of the cerebellum. Describe the morphology of each layer. What makes each layer distinct? Are they made up of different cells? If so, describe the morphology of both of the major cell types as observed under the microscope. Do they contain neuronal processes and connections? If so, describe the connections being made.
   a. Granule cell layer
   b. Purkinje cell layer
   c. Molecular cell layer

Make sure you can identify the following objects and regions in these histological preparations:
a. Granule cells/Granule cell layer
b. Purkinje cells/Purkinje cell layer
c. Molecular cell layer

IV. Cerebral Cortex Golgi Preparation
Slide 70829f (Cerebrum, Cat – Golgi Stained)

Note: The Golgi stain is an old, but poorly understood histological method. Pioneered by Golgi and used extensively by Cajal (neuroanatomy pioneers who won the Nobel prize for their work using the Golgi stain). It has the ability to produce a complete stain of a limited number of neurons. Those neurons that take up the stain will do so throughout the entirety of the neuron (including all of its processes). The result is the preservation of the morphology of a single neuron without the interference of neighboring neurons also being stained. This is a great method for studying the morphology of different types of neurons.

1. Look at a Golgi stain of the cerebral cortex under high magnification. Notice the thin, black, wispy lines running throughout the cortex. These are neuronal processes.
    a. How would you compare the complexity of the cerebral cortex to the cerebellar cortex?
    b. Attempt to identify and distinguish axons from dendrites. How would you explain the difference to your lab partner if he or she were struggling to distinguish between them?
    c. Can you see why dendrites are said to arborize? What does that mean?

V. Horizontal Section of Mouse Brain
Slide Ma521e (Brain of Mouse)

1. Start with low power magnification. Observe the general organization of the brain.
2. Identify the following structures or regions:
    a. Anterior aspect of the brain and olfactory bulb
    b. Posterior aspect of the brain and cerebellum. View the cerebellum. Attempt to identify the different layers. Notice the faintly blue stained areas in the white matter of the cerebellum. What are these structures? What is the functional significance of these structures?
    c. Cerebral cortex. The cerebral cortex is a six-layered structure. Describe the basic inputs/outputs that distinguish the different layers of the cortex.
    d. Hippocampus (look for the sea horse). What is the functional significance of this region of the brain? Describe how the adult neurogenesis that occurs in the hippocampus might be related to its function.

VI. The Retina (V & C, pp. 63-65)
Slide 70713f (Retina from Human Eye)
Slide 70722f (Entrance of Optic Nerve in the Retina)

1. Each of these slides shows a cross section of the neural part of the back of the eye called the retina. The retina is neural tissue. In fact, it develops from an outcropping of the same tissue that forms the rest of the brain. The retina is a multi-layered structure.
    a. The most populated layer contains the photoreceptors that transduce light into neural impulses.
    b. The other layers contain processing cells and output cells (ganglion cells).
2. The axons of the ganglion cells form the optic nerve. They send information from the eye to the brain. The retina appears to have a backwards organization. Light must pass through all of the layers of the retina before reaching the photoreceptors. Once transduced, this information is sent back through the other layers to the ganglion cells on the way to the brain. What advantage does this type of organization afford the photoreceptors?
3. Identify the following structures and describe the function of each:

a. The three main layers of the retina
b. The photoreceptors
c. The optic nerve
d. Retinal pigmented epithelium (RPE)

VII. The Tongue
Slide 70701e (Tongue of Rabbit)

1. Tongue – notice the numerous papillae (like little mountains with valleys in between them).
2. In the valleys are small, rounded, clear objects. These organizations of cells are taste buds. What type of information is transduced by taste buds? In addition to the traditional taste buds, recent evidence supports the existence of two additional taste buds. What type of taste information do these buds convey? Taste is only one component of flavor. What is the other?

B. Assignment 1 Answer Key and Instructor's Notes

Instructor's Note: The student guide and associated questions are listed below in addition to the answers to the questions posed in the guide. All of the answers have been italicized. The answers were written so that they might be either distributed to the student or used solely as supplement for the instructor.

I. Meninges

1. The brain has a three-layered covering collectively called the meninges.
   a. What are the names of each layer starting with the inner most layer and moving out?
   Pia mater, arachnoid mater and dura mater
   b. Name three major functions of the meninges.
   1. Mechanical protection
   2. Vascularization
   3. They provide a fluid filled cushion for the brain to float in which offers protection.
   Capillaries that serve the brain and spinal cord course through all three layers. The subarachnoid space in the arachnoid mater contains cerebrospinal fluid (CSF). There are possible developmental roles for the meninges as well. They may be involved in the guidance of radial glial cells, which serve as guides for migrating cortical neurons, via the release of trophic and tropic factors that allow the positioning of radial glia. Radial glia are vital for the formation of the six layers of the cerebral cortex.
2. Before you remove the meninges, note the cranial nerves emerging mostly from the base of the brain (see V & C, p. 18).
3. Remove the meninges from your sheep brain using scissors and forceps. Be careful not to remove the pituitary gland. Also be very careful in removing the tentorium (the dura that separates the cerebellum and cerebral cortex). Note the thickness and toughness of the two outer layers of the meninges and the fragility of the third layer (which is probably still attached to the brain). Notice how the third layer dips into the sulci, following the contours of the brain.
   a. Which layers compose the tough stuff?
   Dura Mater (literally means tough mother), Arachnoid Mater (means spider-like because it has sublayers with spicules in between its sublayers that give it the appearance of a spider's web).
   b. Which layer is delicate and most closely associated with the brain's surface structures?
   Pia Mater (means tender or small mother).
4. Delicately remove the final layer of the meninges, being careful not to disrupt the cranial nerves on the ventral aspect of the brain.
   a. Which aspect is ventral? Which aspect is dorsal?
   Ventral is the bottom of the brain, dorsal is the top. Remember the dorsal guiding fin on the shark is on its back (dorsal means back). Therefore, the back portions of the spinal cord are dorsal and the front are ventral (venter means abdomen). The central

nervous system (CNS) curves at the brain, so that the dorsal aspect of the spinal cord continues to become the top of the brain.

b. Rostral? Caudal? Anterior? Posterior?

Rostral (meaning "beak") and Anterior are the front. Caudal (meaning "tail") and Posterior are the back.

II. Surface Features of the Brain (V & C, p. 16-17)

1. Attempt to locate the lobes of the brain and review the human counterparts and functions.
   a. What will you use as your landmarks? How do they differ from the human brain?
   In the human brain there are four lobes on each hemisphere of the brain. The longitudinal fissure separates the hemispheres. The central sulcus separates the frontal and parietal lobes. The Sylvian (or lateral) fissure separates the temporal lobe from the frontal and parietal lobes, and the parieto-occipital sulcus separates the occipital lobe from the parietal lobe.
   In the sheep brain the lobes are difficult to identify. The cruciate fissure separates the frontal and parietal lobe, but the occipital lobe boundary is poorly defined and the temporal lobes of the sheep are very small in comparison to the human brain.
   b. Name a primary cortical area contained in each of the four lobes of the human brain.
   The frontal lobe contains primary motor cortex (precentral gyrus). The parietal lobe contains primary somatosensory cortex (postcentral gyrus). The occipital lobe contains primary visual cortex. The temporal lobe contains the primary auditory cortex (Heschel's gyrus in the superior temporal gyrus near the insular cortex). Primary gustatory cortex is found in the insular cortex underneath the frontal and parietal opercula and deep to the lateral (Sylvian) fissure.
2. What is the difference between a sulcus and a fissure? A sulcus and a gyrus?
A sulcus is a shallow groove, a fissure is a deep groove, and a gyrus is a ridge or bulge on the surface of the brain.
3. In the human brain, what is the name of the gyrus that contains the primary motor cortex? The primary somatosensory cortex?
The Precentral Gyrus and the Postcentral Gyrus, respectively.
4. Gently lift and pull the cerebellum caudally, being careful not to pull too hard, and gently pull the cerebral cortex rostral. Observe the corpora quadragemina.
   a. What structures compose the corpora quadragemina?
   The superior and inferior colliculi on each side of the brain (total of 4 = quadra).
   b. What's another name for these structures?
   The tectum or the roof of the cerebral aqueduct.
   c. What lies immediately ventral to these structures?
   The cerebral aqueduct.
   d. What is the function of these structures?
   Sensory component of the midbrain that is involved in visual (superior) and auditory (inferior) processing/orienting behaviors.

III. Ventral View (V & C, p. 18)

1. Identify as many of the cranial nerves as you can see (note: the cranial nerves are delicate and many will not survive your dissection of the meninges).

a. What do they do (generally)?
Sensory and motor functions for the head and neck, which include olfaction and the visual senses. Many cranial nerves control eyes movements and those required for mastication and speech (the articulators). Consider the importance of being able to control eye movements and why there are so many muscles and nerves that serve these muscles. Some have special sensory features (e.g., cranial nerves I are the olfactory bulbs and II are the optic nerves). There may even be a Cranial Nerve Zero (a.k.a the terminal nerve) in humans, which is the subject of a future assignment. This nerve may be involved in pheromone signaling. Try the following mnemonic device to remember the function of some of the nerves: You have ***1*** *nose,* ***2*** *eyes, and* ***3, 4, 6*** *makes my eyes do tricks!*
b. Name each of the 12 cranial nerves in order starting with cranial nerve I.
Try the following mnemonic device to remember the 12 cranial nerves: **O**n **O**ld **O**lympus' **T**owering **T**ops **A** **F**riendly **V**iking **G**rew **V**ines **A**nd **H**ops

2. Mammillary Body (MB)
   a. What is it connected to?
   Via the fimbria/fornix, the MB is connected to the hippocampus and is part of the larger limbic system.
   b. Why might Korsakoff's syndrome, which targets the mammillary bodies, result in anterograde amnesia?
   Korsakoff's syndrome can be caused by Vitamin B1 (thiamine) deficiencies resulting from malnutrition often due to alcoholism (alcoholics may consume all of their calories via alcohol ingestion, which is high in calories but lacking in nutrition – it also hinders the absorption of some nutrients). The result is a degeneration of the MB (and other brain regions) and malfunction of the limbic memory circuit. The hippocampus is involved in consolidation (transfer of short-term memory into long-term memory) especially for explicit/declarative memories and provides projections to the mammillary bodies via the fornix. Therefore, the individual may lose the conscious ability to learn new information. Dr. Oliver Sacks (1985) described such a case in his book The Man Who Mistook His Wife for a Hat. *The story is called "The Lost Mariner."*
3. Infundibulum
   a. It connects _____ to _____.
   Also known as the pituitary stalk, it is the connection between the hypothalamus and pituitary gland.
   b. What is so important about this connection?
   This connection helps the brain control many distant organs as well as the autonomic nervous system via the direct release of hormones (oxytocin and vasopressin) and the regulation of hormone release from the pituitary gland (a.k.a. the master gland). This is a major neuroendocrine connection and helps to regulate body temperature, appetite, circadian rhythms, sexual activity, emotions, etc.
4. Optic Tract/Chiasm – this is where part of the visual world decussates (see V & C, pp. 89; 101-103 for additional help).
   a. What does decussate mean?
   The word decuss derives from the Latin word decussare, which means to divide crosswise, or in the form of an X. Projections that originate on one side of the

body/brain and terminate in the other are said to decussate. Many sensory and motor fibers decussate so that the left half of the body is controlled by the right motor cortex and the right somatosensory cortex processes information from the left half of the body.

b. Which parts of the eye decussate?

The projections from the nasal retina will decussate whereas the temporal retina projections will not.

c. How does the fact that some processes decussate and others do not determine the location of the left vs. the right visual fields?

The nasal retina provides information from the ipsalateral (same side) visual field, whereas the temporal retina provides contralateral visual field representations. Therefore all of the information about one half of the visual world will project to the contralateral (other side) visual cortex (e.g., the left visual field is mapped on the right visual cortex).

5. Olfactory system (refer to V & C, p. 93 for additional help)

a. Where are these sensory projections sent in the brain?

The olfactory bulbs send information directly into evolutionarily old areas of cortex (e.g., the entorhinal cortex) and directly into limbic regions (the hippocampus and amygdala).

b. What is the first major stop of other sensory projections in the brain (Hint: it is part of the diencephalon)?

The thalamus (a Greek word meaning inner chamber) is the first major stop of many afferents. It is involved in organizing, some processing, and relaying sensory information to appropriate cortical areas. It is appropriate the think of the thalamus as a relay nucleus, but it has many other important functions.

c. What are some of the implications for the unique projection pattern for olfactory sensory fibers?

The sense of smell has direct access to memory and emotional regions of the brain and can elicit both strong memories and strong emotional reactions, possibly more so that other sensory systems. There are many possible evolutionary explanations for this specialization that would include identification of good food sources and appropriate mates. Pheromones and the Major Histocompatability Complex (MHC) are thought to signal appropriate mates and to be received through special olfactory mechanisms that involve the accessory olfactory bulb in some animals and analogous structure in others. The MHC is used for self/non-self recognition. Foreign antigens will be recognized as non-self and attacked by the immune system. One theory holds that potential mates are selected based on an ability to detect a compatible immune system. What is your first memory? Mine is the smell of mint that surrounded the house we lived in when I was 2. The smell of a particular shampoo still elicits negative emotional reactions of an ex-girlfriend and a relationship that ended badly. Memories and smells are often commingled.

6. Temporal Lobe

a. Name two limbic structures that are located deep within the temporal lobe.

The hippocampus (memory consolidation) and the amygdala (emotional processing) are part of the limbic system.

IV. Midsagittal View (V & C, pp. 21-22)

1. Spinal Cord, Medulla, and Pons
   a. These are contiguous structures. How are they similar? How are they different?
   All of these structures contain ascending (afferent) and descending (efferent) fiber pathways. The pons is the most rostral of these structures and is visible as a large bump on the ventral portions of the brainstem. Pons, meaning "bridge," has many connections to the cerebellum. Therefore, it is an important structure for movement and posture control. The medulla oblongata is the most caudal portion of the brainstem; it contains much of the reticular formation as well as many nuclei that control vital functions such as respiration and heart rate. The reticular formation is a group of nuclei that are collectively involved in arousal states (and sleep). Many of the motor fibers leaving the brain decussate at the medullary pyramids. The spinal cord is the information superhighway. It contains segmented ascending (sensory) and descending (motor) pathways that are organized based on topography as well as based on the type of information being sent (e.g., pain, pressure, temperature).
   b. What developmental division of the brain do these structures develop from?
   The pons and medulla are both considered hindbrain structures because they develop from the rhombencephalon, but the rhombencephalon further segments during development. The pons develops from metencephalon and the medulla from myelencephalon. The spinal cord develops from the most caudal aspects of the neural tube.
2. Midbrain
   a. What are the six major nuclei that make up the midbrain?
   Inferior colliculus (IC), superior colliculus (SC), substantia nigra (SN), ventral tegmental area (VTA), red nucleus (RN), and periaqueductal gray area (PGA).
   b. What are the major functions of these nuclei?
   IC = auditory processing, SC = visual processing, SN = voluntary movement, VTA = reward, RN = motor coordination, PGA = pain modulation.
   c. In general, what is the overall function of the midbrain?
   It is involved in processing sensory inputs and providing orienting movements or responses. For example, if you see movement out of the corner of your eye, you might move your head and eyes in that direction for further processing of the visual information. In this example, you orient to the visual stimulus by turning towards it so that you can experience it with your central vision (i.e., with high visual acuity cones vs. low visual acuity rods that compose most of your peripheral vision).
3. Diencephalon
   a. The diencephalon is made up of which two major structures?
   The thalamus and the hypothalamus. However, other important structures also develop from this forebrain division. For example, the epithalamus, including the pineal gland (or epiphysis), which produces melatonin and is involved in circadian rhythms, and the posterior portion of the pituitary gland (or neurohypophysis), which secretes oxytocin and vasopressin, are both components of the diencephalon.
   b. The name of one of these diencephalon structures suggests its anatomical position in relation to the other. Which structure? What direction is provided by the name?
   <u>Hypo</u>thalamus suggests that it is under the thalamus.

c. What are the major functions of each of the two structures of the diencephalon?
The thalamus is the major relay nucleus of the brain that organizes and processes ascending sensory information before relaying it to cortical areas and descending motor information before relaying it down motor tracts. Thalamus comes from a Greek word meaning inner chamber, and it literally acts as a funnel for incoming and outgoing fibers. The hypothalamus is a major control center for the neuroendocrine system as suggested above and as such regulates many endocrine and autonomic functions. It is also part of the limbic system.

4. Cerebral Cortex - make sure you can locate the different lobes and surface features of the human brain from pictures in your textbook. Try to locate analogous regions in the sheep brain (see V & C, p. 81 for additional help).
   a. What primary sensory cortical area is located in the temporal lobe?
   Heschel's gyrus or the primary auditory cortex is found in the superior temporal gyrus of the temporal lobe. It is buried deep in the lateral (Sylvian) fissure adjacent to the insular cortex (insula means covering); the insular cortex contains the primary gustatory cortex.
   b. Which lobe is anterior to the parietal lobe? What primary cortex is contained in this lobe and, therefore, what are some of the major functions of this area?
   The primary motor cortex is found on the precentral gyrus of the frontal lobe (rostral to the central sulcus). The primary somatosensory area is located on the other side (caudal) of the central sulcus in the parietal lobe. The frontal lobe contains the primary motor areas as well as many motor association areas and Broca's area. Broca's area is specialized for speech production and controls many of the articulators whose shapes help to determine the sound that is produced as air passes by them. Many of the motor association areas aid in planning movements or responses.
   c. Which lobe contains the primary visual area? What are the functional consequences of damage to the primary visual area compared to the visual association areas?
   The occipital lobe. The occipital lobe also contains a large number of visual association areas as does the temporal and parietal lobes. Damage to the primary visual cortex will likely result in some form of blindness, but damage to a visual association area can cause deficits in specific visual modalities and culminate in more specific types of visual deficits or deficits in visual perception (e.g., damage to the fusiform face area in the superior temporal lobe can result in prosopagnosia or an inability to recognize faces, whereas damage to V4 on one side of the brain can result in hemi-achromatopsia or loss of the ability to perceive color in one half of the visual field).
5. Cerebellum
   a. What happens to an animal when you damage its cerebellum, and what does this suggest about one of the major functions of the cerebellum?
   It depends on where the lesion occurs, but common symptoms include ataxia (loss of balance), asynergia (loss of smooth movement), and dysmetria/hypermetria (underestimating/overestimating the distance of an object). The cerebellum, therefore, is involved in the coordination of muscle groups based on on-the-fly sensory feedback. This type of processing is necessary when performing ballistic

movements (such as throwing a baseball). Therefore, these types of movements will be very uncoordinated.

b. Cerebellum means small brain – look at its organization and suggest why.

It is a three layered structure with white matter on the inside and grey matter on the outside. There are lobules instead of lobes. There are major inputs (via the cerebral peduncles) and outputs (via deep cerebellar nuclei). In many ways it operates as a mini-brain or information processor.

6. The Ventricular System
    a. Identify and name the different ventricles, the regions of the brain they serve and related components. Describe how the different ventricles are interconnected to allow a flow of cerebrospinal fluid (CSF). Be sure to include the following terms in your answer: the Lateral, third, and fourth ventricles; the septum pellucidum; the interventricular foramen; and the cerebral aqueduct.

The Lateral Ventricles are Ventricles I and II. They are separated by a thin membrane called the septum pellucidum. At the base of the septum pellucidum is a group of nuclei called the septal nuclei that have important limbic functions. The lateral ventricles serve the telencephalon (cerebral cortex, basal ganglia and limbic system). The lateral ventricles are connected to the third ventricle (III) via the interventricular foramen (Foramen of Monro). The third ventricles serve the diencephalon. The third ventricle is connected to the fourth ventricle (IV) via the cerebral aqueduct. The cerebral aqueduct is a useful landmark for the midbrain because the roof of the cerebral aqueduct is the tectum and its floor is the tegmentum. The third ventricle serves the diencephalon. The cerebral aqueduct serves the midbrain and the fourth ventricle serves the brainstem and the cerebellum. From the fourth ventricle the CSF can flow to the central canal of the spinal cord or the subarachnoid space of the meninges via three foramens (Foramen of Magendie and the two Foramen of Lushka). CSF eventually travels to the superior sagittal sinus where it is reabsorbed into the venous system.

b. What is so important about the ventricular system and the CSF that it contains?

It absorbs shock, provides nutrients, eliminates waste products, and redistributes the weight of the brain as it floats in this aqueous solution. Historically, philosophers thought that it contained the anima (mind) spirit and that flow through the CSF, which was thought to be responsible for all brain functions. Infection, disease, or damage to the ventricular system can produce meningitis, ventriculitis, or hydrocephalus. Dysregulation of the pressure within this closed system can result in neurological symptoms and eventual brain damage. For some patients, dysregulation of the ventricular pressure can be alleviated by the insertion of an artificial shunt at the base of the brain with an under-the-skin tube draining excess fluid into the peritoneal cavity.

c. Where is the CSF made?

It is made throughout the ventricular system by specialized ependymal cells called the choroid plexus. It is a renewable resource as it is eventually reabsorbed by the body and eliminated. Ependymal cells are a type of glia cell. Ependymal cells are similar to cells in the rest of the body that line our internal organs.

7. Cingulate Gyrus
    a. I am calling your ATTENTION to this structure – Why?

The cingulate cortex is a limbic structure with many simple and complex functions including emotional processing, learning, memory, and executive control features. Researchers speculate that the anterior portion of the cingulate cortex (ACC) is involved in reward anticipation and controlling the limited resource of attention and its division when a task demands high level cognitive processing. ACC is thought to be overactive in Attention Deficit Hyperactivity Disorder.

b. Which brain system does the Cingulate Gyrus belong to?

The limbic system.

c. What does this suggest about another of its functions?

It processes emotional stimuli, especially in the dorsal portions of the cingulate cortex.

8. Corpus Callosum (CC)

a. It is a commissural system – what does this mean and what does it connect?

Commisures connect the hemispheres of the brain. The CC is the largest of the commissural systems as its name implies (it means great body). Generally speaking, each region of the CC connects the same areas of the cerebral cortex in each hemisphere to one another. It is composed of white matter, meaning that the connecting fibers are myelinated. From rostral to caudal, the parts of the CC are the rostrum, genu, body, and splenium. These portions of the CC are useful landmarks when viewing brain sections. Immediately dorsal to the CC is the cingulate cortex and the lateral ventricles are ventral to the CC.

b. Name the other commissural systems.

The massa intermedia connects the halves of the thalamus. The anterior commisure helps to connect the two temporal lobes and the posterior commisure connects midbrain and diencephalon structures.

9. Massa intermedia - what does it connect?

The massa intermedia connects the halves of the thalamus.

10. Hippocampal formation (if you can see it): Hippocampus means sea horse.

a. What happened to HM when he lost this structure?

HM had radical surgery that involved removal of the hippocampus to cure his otherwise untreatable seizure condition. He developed what seemed to be complete anterograde amnesia.

b. What does the loss suggest about the function of the hippocampus?

He was able to carry on a conversation, but could not remember that conversation even minutes later, suggesting that his deficit was limited to creating new long-term memories and not involving short-term stores. Interestingly, his amnesia was later found to less severely involve implicit or procedural memories and to more severely affect explicit/declarative memories. The hippocampus is involved in consolidating short-term memories into long-term memories and specifically for explicit information (especially relational/spatial information). In the motion picture Memento (2000), the protagonist (Guy Pierce) develops anterograde amnesia due to trauma that damages the hippocampus.

11. Tectum (roof)

a. What two structures compose the tectum?

The roof of the cerebral aqueduct contains the superior (SC) and inferior colliculi (IC). Together the inferior (2) and superior colliculi (2) on both sides are called the corpora quadragemina (four bodies).

b. Which sensory systems project to which colliculi?

Auditory to the IC and visual to the SC.

c. Without looking in your book, which colliculus is closer to the dorsal aspect of the brain, the superior or inferior? Explain how you came to your answer.

Remember the previous discussion concerning dorsal/ventral aspects of the spinal cord and brain. The SC is more dorsal (towards the top) to the surface of the brain.

12. Tegmentum (floor)

a. Name several nuclei contained in the tegmentum.

The floor of the cerebral aqueduct contains many nuclei: the substantia nigra (SN), red nucleus (RN), ventral tegmental area (VTA), periaqueductal grey (PAG), etc.

b. Two of the nuclei in the tegmentum are dopaminergic. Name the nuclei and explain what dopaminergic means.

They are the SN and VTA. Dopaminergic means that these nuclei (group of cell bodies) send their electrochemical signals by releasing the neurotransmitter dopamine into the synapse.

c. Which dopaminergic nucleus in the tegmentum degenerates in Parkinson's disease, and which one is involved in drug addiction?

Parkinson's disease targets the substantia nigra (pars compacta). These neurons degenerate and produce severe motor impairments including resting tremor, bradykinesia (slowed movement) and postural instability. The disease symptoms are not present until approximately 70% of these dopaminergic neurons have degenerated. Many drugs of abuse increase the release of dopamine from the ventral tegmental area to its connections in the nucleus accumbens and prefrontal cortex. The stimulation of these postsynaptic regions and the associated release of dopamine are related to euphoria, self-reported "high" and reward anticipation after exposure to drugs or natural reward (food, sex). Repeated drug exposures are thought to induce compensatory changes in these brain regions leading to an addiction syndrome.

d. Which nucleus is involved in pain perception?

The PAG regulates pain perception through the modulation of descending pain pathways that project to the spinal cord. PAG stimulation can reduce the pain signal that is traveling from the periphery to the brain via the regulation of neurotransmitters and opioid peptides. Reducing the ascending pain signal also reduces the perception of pain. Electrical stimulation of the PAG in animals can produce complete analgesia.

13. Anterior Commissure (AC) and Posterior Commissure (PC)

a. What good are they?

See the answer to 8b in IV (midsagittal view) above. The AC connects the temporal lobes of the two hemispheres and the PC connects midbrain and diencephalon structures.

14. Pineal gland

a. What is its historical significance?

Many philosophers, such as Descartes, thought that the pineal had mystical properties. Due to its position in the relative middle of the brain and Descartes' incorrect observation that it was one whole structure rather than being bisected like other midline structures, he though that it was the seat of the soul-- the juncture of mind/body dualism. According to Descartes, a differential flow of animal spirits, which is controlled by the pineal, causes changes in interfibrillar spaces, thus originating conscious awareness such as cognitions or sensations. The pineal gland is where he thought the soul contacts the body to induce such changes.

b. What is it now known to do?

Release melatonin, which is involved in the regulation of circadian (about a day) rhythms. Circadian rhythms drive many homeostatic functions including sleep.

V. Special Dissections (V & C, pp. 23-26)

Do not try to replicate these dissections, but use the pictures to help understand the 3-D organization of the brain and the following structure-function relationships:

1. Visualize how information from the optic tract flows first to the relay nucleus (thalamus) and specifically to the lateral geniculate nucleus.
   a. Why is it called the geniculate nucleus? What does it look like?
   Given the appropriate tissue preparation it resembles a bent knee (geniculate) such as when one genuflects or goes to bent knee to honor another.
   b. These fibers are relayed to three major regions of the brain. Indicate what the information might be used for within these structures:
      i. Suprachiasmatic nucleus of the hypothalamus
      These fibers provide light information to the hypothalamus to entrain (reset) the circadian clock. Anything that resets the clock is called a Zeitgeber (or "time giver").
      ii. The Superior Colliculus
      These fibers provide information necessary for making orienting movements towards sensory stimuli. Bats use it for echolocation.
      iii. The Occipital Lobe
      Information relevant to visual perception is sent through this projection, including information about contrast, brightness, contours, shape, spatial resolution, color, movement, and so forth.
   c. What is the thalamic division that relays auditory information?
   The medial geniculate nucleus. Other divisions of the thalamus relay other types of sensory information (e.g., the ventral posterior division for somatosensory information).
   d. Name the main destination for auditory information after the leaving the thalamus.
   The primary auditory cortex in the temporal lobe (Heschel's Gyrus).
2. Notice the internal capsule which contains fibers coming to the brain and fibers going from the brain. These fibers all converge near the thalamus. Because these projection fibers splay out (diverge) into cortical regions, they are called the optic radiations.

VI. Cross Sections (refer to V & C, p. 28, for help in determining where to section)

1. Coronal section through the optic chiasm (Section E in V & C, on p. 33)

a. Gray matter and white matter

i. What makes matter gray versus white?

See answer below.

ii. What cell type makes the white stuff?

See answer below.

iii. What is the physiological significance of the white stuff?

Myelin. Gray matter is made up of nuclei (groups of cell bodies) and unmyelinated axons. White matter is made up of myelinated axons. In the brain, gray matter is found on the outside and white matter (myelin) is found on the inside. Myelin is produced by oligodendrocytes in the CNS and by Schwann cells in the peripheral nervous system (PNS). Both cell types are glia cells. Myelin is a white fatty substance that is contained in the processes of the glia cell. Oligodendrocytes and Schwann cells myelinate axons by wrapping their processes around them. The myelin acts as an insulator and increases resistance of the electrochemical signal in the axon, resulting in an increased passive flow of the action potential (AP) in myelinated axons compared to unmyelinated axons. Because AP regeneration takes time, the myelinated axons will propagate the AP much more rapidly. Also, the number of active AP regeneration events is reduced by the increase in passive flow capability produced by the myelin. Myelinated axons regenerate the AP at regular intervals at specialized, unmyelinated areas of the axon called Nodes of Ranvier. The nodes contain large quantities of voltage-gated sodium channels that initiate the all-or-nothing membrane potential changes known as the AP. Because the signal appears to be jumping from node to node, it is called saltatory (to jump) conduction.

b. The Striatum

i. Which two nuclei make up the striatum?

The striatum is made up of the caudate nucleus and the putamen. Caudate means tail and the caudate nucleus has a tail that trails from forebrain regions towards the midbrain in an arching fashion. Collectively they are called the striatum because they have striations or stripes due to the commingling of these two nuclei and because of the fiber bundles that run through these sections (striatopallidonigral bundles). Technically, the ventral striatum (better known as the nucleus accumbens) should also be included in the term striatum.

c. Globus pallidus along with the striatum forms the basal ganglia (BG).

i. What is the general function of this brain circuit?

Although these nuclei have a large variety of functions including emotive, cognitive, and learning, they are best recognized for their involvement in motor control.

ii. Name two neurodegenerative disorders that target this brain circuit.

Parkinson's disease attacks the substantia nigra, which is a major input into the striatum, and Huntington's Chorea targets cells directly in the striatum. Parkinson's disease affects the motor circuit of the BG by decreasing its ability to excite the motor cortex. Huntington's Chorea affects the BG by increasing its ability to excite the motor cortex. So with Parkinson's disease, one acquires paucity of movement and with Huntington's Chorea, one acquires an excess of movement (Chorea means dance-like).

d. Internal/External/Extreme Capsule and corona radiata are all fiber pathways sending information to and from the cerebral cortex.
e. Corpus callosum
   i. What does corpus callosum mean?
   Great body (see IV. 8. above).
   ii. What is the structure immediately ventral to the corpus callosum?
   Lateral ventricles (see IV. 6. above).

2. Coronal section through the mammillary body (Section G in V & C, p. 35)
   a. Thalamus
      i. Attempt to locate the different divisions of the thalamus discussed at IV. 3.
   b. Hippocampal formation
      i. What is the general function of the hippocampus?
      See IV. 10. Consolidation of short-term memory, specifically for explicit-declarative, relational, or spatial information.
      ii. What does hippocampus mean? Can you see why?
      Hippocampus means sea horse.
   c. Amygdala (means almond)- it's all the RAGE
      i. What might happen if you lesion someone's amygdala?
      The dysregulation of emotional processing, especially for the emotions of fear and anger. The amygdala is part of the limbic system and sends direct connections to the hypothalamus to control autonomic responses that we recognize as emotional responses.
   d. Lateral Ventricle
      i. What number ventricle is this?
      Trick question! Either Ventricle I or II. They are both lateral ventricles and you do not need to distinguish between them.
   e. Limbic or Cingulate Cortex (located superior to the cingulum and corpus callosum)
      i. Name at least one function associated with this structure.
      Emotional processing, allocation of attentional resources and impulse control.

3. Coronal section through the cerebral peduncle (Section H in V & C, p. 36)
   a. Hippocampus & dentate gyrus
   b. Lateral geniculate nucleus (part of the thalamus)
   c. Substantia nigra
      i. What neurotransmitter is used by this nucleus?
      Dopamine
      ii. What neurodegenerative disorder targets this structure?
      Parkinson's disease.
      iii. What forebrain nuclei does this target project to?
      Corpus striatum (caudate and putamen).
      iv. What is the function of this nucleus?
      Regulation of voluntary movements.
   d. Superior Colliculus

VII. Horizontal Brain Sections (refer to V & C, pp. 29-30):

Horizontal sections demonstrate the three dimensionality of the brain, providing an overview of the location of most structures in relation to one another.

VIII. Spinal Cord Sections

Use V & C (p.105), text book, and lecture notes to help you locate the following portions of the spinal cord:

1. Gray matter, white matter, and central canal
    a. How is the organization different from the brain's organization?
    The organization is opposite to the brain's, with the white matter on the outside and the gray matter on the inside. The gray matter contains, among other things, interneurons and motoneuron cell bodies. Interneurons connect projection neurons. For example, they connect sensory neurons to motor neurons, which make reflexes possible. Consider the stretch reflex that occurs when a heavy weight is unexpectedly placed onto an outstretched hand. The weight will stretch the muscles in that arm as the arm drops due to the weight. The receptors on the muscle that detect the muscle fiber stretch and joint displacement will be activated and the impulse will be sent to the spinal cord. In the spinal cord, interneurons connect this sensory fiber to motor fibers. The result is the activation of the motoneurons and muscle fiber contraction to correct for the unexpected change in arm position. This action and reaction occurs at the level of the spinal cord without direct involvement of the brain. Motoneurons are multipolar neurons with cell bodies in the spinal cord. The white matter in the spinal cord is fasciculated. These segments carry different information based on type of information (motor vs. sensory, type of sensory receptor, etc.) and area of the body it is going to or coming from.
    b. What is in the central canal?
    Cerebrospinal fluid.
    c. What brain system is the central canal continuous with?
    The ventricular system. The central canal is connected to the fourth ventricle via several foramina.
2. Dorsal horn versus ventral horn
    a. Which way is dorsal and which way is ventral in the spinal cord?
    Remember the dorsal guiding fin on the shark. It is on its back or dorsal surface. The belly side is the ventral side.
    b. Why is this different from the orientation of the brain?
    Remember that the CNS curves once you reach the brain so that the dorsal axis becomes the top of the brain.
    c. Which horn contains the cell bodies of the motoneurons?
    The ventral horn. Remember that there is a dorsal root ganglion, but no ventral root ganglion because the cell bodies of the motor system are contained within the spinal cord.
    d. What type of neuron is a motoneuron (i.e., describe its morphology)?
    Multipolar. In other words, it has many projections emanating in all directions.
    e. Where are the cell bodies of the sensory neurons?
    They are found in the dorsal root ganglion (DRG), outside the spinal cord. A group of cell bodies in the PNS is called a ganglion.
    f. What type of neurons are these sensory neurons (describe their morphology)?

These sensory neurons are unipolar, which means that they have one process emanating from the cell body, which bifurcates (splits in two directions). One process travels towards the skin or muscle. The other travels towards the spinal cord. This one process serves as both a dendrite (to collect information) and an axon (to transmit information). Actually, these neurons are pseudounipolar because the dendrite acts more like an axon. The dendritic part of the process contacts a sensory receptor. When the receptor transduces sensory information, the dendritic process initiates and propagates an action potential, which does not decay on its way to the axonal process.

3. Dorsal root versus ventral root (One of each serves the same basic region of the body and enters/exits the same area of the spinal cord; they are called spinal nerves).
    a. What type of fibers make up the dorsal root (sensory/motor)?
    The fibers in the dorsal root are the axonal processes from the unipolar (pseudounipolar) neurons contained in the DRG. Therefore, they carry sensory information to the CNS. Fibers sending information towards the brain/CNS are called afferents (<u>a</u> in Latin means "to" or "towards").
    b. What type of fibers make up the ventral root (sensory/motor)?
    The ventral root carries the fibers from the ventral horn, which is where the motoneuron cell bodies reside. Therefore, the ventral root carries motor information from the CNS. Fibers carrying information from the brain/CNS are called efferents (<u>e</u> in Latin means "from").
4. Spinal Nerve (see 3. above). Describe the organization of the spinal cord into functional segments or spinal nerves. How many spinal nerves are there and how are they grouped?

A spinal nerve is made up of a collection of dorsal (sensory) and ventral (motor) fibers for a segment of the body on one side of the body. There are 31 pairs of spinal nerves, with each part serving a particular part of the body. Each spinal nerve and the area of the body from which it receives sensory information are depicted in a dermatome map. Starting from the caudal aspects and moving in the rostral direction the pairs of nerves are as follows: 1 coccygeal, 5 sacral, 5 lumbar, 12 thoracic, and 8 cervical pairs of nerves.

  a. Would there be a greater deficit after cervical or lumbar spinal cord damage?
  Cervical.
  b. Why?
  Damage occurring to any portion of the spinal cord will affect all of the fibers that must pass through that section (both afferents and efferents). The lumbar spinal cord is more distal (relative to the brain) than the cervical, which is more proximal. Therefore, most fibers, regardless of their origin in or destination to the body, will pass through the cervical spinal cord on the way to or from the brain (notice the enlargement of the cervical regions of the spinal cord). On the other hand, only information going to or coming from the waist and lower will need to pass through the lumbar cord region.

5. Dorsal Root Ganglion (DRG)
    a. What's in the DRG?
    Unipolar (pseudounipolar) cell bodies.
    b. Why are there no ventral root ganglia?
    Because the motoneuron cell bodies are in the spinal cord (ventral horn).

Microscopic Anatomy (Histology of Sensory and CNS Tissue)
Make sure to handle these glass microscope slides very carefully – they will break if you mishandle them.

I. Spinal Cord Sections (V & C, pp. 50-55):

Slide 70812e (Spinal Cord, Human – for general structure)
Slide Ma527e (Spinal Cord of Cat – stained for Nissl bodies)
Slide HE2-22 (Spinal Cord of Cat – Dorsal Root Ganglion Section)
Slide 70825f (Spinal Cord of Cat = light blue stain)

1. Locate the ventral horn of the spinal cord by first finding the motoneurons. Note: Depending on the tissue preparation that you have, you may only be able to see the soma and short stubs of the multiple processes. This will cause them to appear star shaped. They are clearly confined to one horn of the spinal cord – the ventral horn. Although you may see some nuclear staining in the dorsal horn, these cells are not as large and not multipolar in shape. Once you have found the motoneurons, move to the 10x objective for a closer look.
    a. What shape do they have?
    Motoneurons are multipolar.
    b. How are they different from the sensory neurons in the DRG?
    The sensory neurons are unipolar or pseudounipolar neurons.
2. Can you see the divisions of the white matter? What is the functional significance of these divisions? Note: Position the slide so that you are viewing the border of the spinal cord. The columns/fascicules should appear as delicate partitions. In fact they have small membranes that separate them from other surrounding columns/fascicules, almost like the sections of an orange (refer to V & C, pp.71-73; 77 for additional help).

These are fiber tracts coming from and going to particular regions of the body, and they are carrying particular types of information. Each column/fasciculus of the spinal cord is carrying specific motor commands from the brain to a particular area of the body (efferents) or specific sensory information from the body to the brain (afferents).

Make sure you can identify the following structures in these histological preparations:

a. Gray matter and white matter

b. Ventral and dorsal horn: Note: The horns contain myelinated fibers (on the inside) and are the white matter with gray matter surrounding.

c. Dorsal root ganglion in some slides: Note: Position the slide so you are viewing outside of the spinal cord. The dorsal root ganglia may appear as a separate, round tissue structure with many stained nuclei. The DRG contain sensory neurons.

d. Motoneurons

e. Central Canal: Note: The central canal is in the very center of the spinal cord and is absent any staining, save the dark staining of the ependymal cells (specialized glia) that line the canal and, occasionally, also the choroid plexus (specialized glia that produce CSF).

II. Nerves (V & C, pp. 56-57)

Slide 70818e (Nerve, Human – cross section)
Slide HE3-11 (Nerve, Peripheral – cross section)

Slide 70817e (Nerve, Human – transverse section)

1. What is the definition of a nerve?

A nerve is a grouping of axons. In the cross sections, note the small circular objects – each one is an axon. Each axon has a myelin sheath around it.

Note just how many fibers are contained within a given nerve segment. Many of these axons are myelinated. The myelin is only faintly stained, but the axon is darkly stained and located in the center. Note the segmentation of this tissue and the connective tissue that separates various segments. Some blood vessels can be seen as they course through the connective tissue.

2. The transverse section shows the length of the individual axons. You can still see the myelin sheath around the axon. Under high magnification, notice how the myelin is absent around very small regions of the axon. These are the Nodes of Ranvier.
    a. What occurs at these Nodes?

    Nodes of Ranvier are where the action potential (AP) is regenerated. Remember that the AP is an electrical signal that decays and must be regenerated at regular intervals. In myelinated axons the decay is much slower due to the increased size and resistance of the axon. Therefore, the signal passively flows a greater distance down the axon and needs to be actively regenerated less frequently. Active regeneration of the AP takes time, which means that myelinated axons propagate their signal more rapidly than unmyelinated axons. A large number of voltage gated sodium and potassium channels are located in the Nodes of Ranvier that operate in the same fashion as they do at the axon hillock (i.e., a tightly regulated series of channel gating that produces the characteristic membrane potential changes called the AP). Once regenerated at a Node of Ranvier, the AP will passively flow to the next node, where it is again regenerated. Because the signal appears to jump from node to node, this is called saltatory conduction.

    b. What is the purpose of the myelin sheath?

    It serves as an insulating factor to reduce decay of the AP and, therefore, to increase the passive flow of the electrical signal, resulting in rapid conduction.

    c. Which cells make the myelin in the CNS? In the PNS?

    In the CNS it is the job of an oligodendrocyte to myelinate segments of several different axons at a time, by wrapping their myelin-containing processes around the axon. In the PNS myelination is the job of the Schwann cell. Each Schwann cell myelinates only one axon. Both Schwann cells and oligodendrocytes are glia cells.

    d. If myelination is so beneficial, how come all axons are not myelinated?

    It's probably a space issue. If all fibers in the body were myelinated, we'd probably have to give up important cortical tissue and, besides, our spinal cord would probably be the size of a small tree trunk.

    e. What are some types of fibers that are likely to be myelinated? That is, what type of neural signals would likely need a fast reaction?

    Pain fibers (spinothalamic) and other sensory feedback fibers as well as the motor fibers that control the responses to these sensations are some examples of myelinated fibers.

Make sure you can identify the following objects in these histological preparations:

a. Axons
b. Myelin sheaths
c. Nodes of Ranvier: Note: To see the Nodes, look in the transverse section and use high magnification (greater than a 10x objective may be necessary). You are looking for a thinning and then absence of the myelin sheath around the axon. Spend some time looking for it; it is worth the search.

III. Cerebellum (V & C, p. 60-61)
Slide 70803e (Cerebellum, Human)
Slide HE1-32 (Cerebellum, Human)

1. Observe the difference between the cerebral cortex (V & C, p. 58) and the cerebellum. Notice that each structure is made up of diverse cell types organized into layers. Using your text, describe how the cerebellum modulates movements based on the sensory signals received. Which part of the cerebellum receives the sensory signals? How do these sensory signals influence the output of the cerebellum? What is the result of the cerebellar output on the motor cortices?

The cerebellum and its relatively simple, three-layered structure provide an excellent example of a simplified functional microcircuit. The cerebellar cortex modulates activity of the deep cerebellar nuclei, which send projections to the premotor areas. These projections carry sensory information into the cerebellar cortex to the Purkinje cells. Several computations are performed, resulting in the regulation of the strong inhibitory signal sent by the Purkinje cells to the deep cerebellar nuclei. Therefore, sensory feedback modifies the motor program resulting in smooth, coordinated movement. Almost every synapse in the cerebellum undergoes synaptic plasticity, which allows for fine-tuning of movements and forms the basis of motor learning.

2. Observe the three different layers of the cerebellum. Describe the morphology of each layer. What makes each layer distinct? Are they made up of different cells? If so, describe the morphology of both of the major cell types as observed under the microscope. Do they contain neuronal processes and connections? If so, describe the connections being made.
   a. Granule cell layer
   Made up of small, round granule cells, these are stained dark blue. The cerebellar granular cells are the most abundant cell type in the whole brain. Humans are thought to have 10^{10} granule cells in the cerebellum (approximately 70% of all neurons in the brain and spinal cord combined). Granule cells are also found in other regions of the brain (e.g., the hippocampus).
   b. Purkinje cell layer
   Made up of large Purkinje cells, these big cells border the granule cells, but lie close to the molecular cell layer. Purkinje cells are among the largest cells in the CNS and have very interesting dendritic arbors, which form almost 2-D layers through which the granule cell processes pass. The arborization of Purkinje cell dendrites makes for striking pictures. Each Purkinje cell receives up to 200,000 granule cell synapses but only one powerful synapse from climbing cell fibers originating in the inferior olive of the medulla. Purkinje cells are the only output cell from the cerebellar cortex. They project to deep cerebellar nuclei and are vital for motor coordination. Cerebellar

Purkinje cell degeneration results in severe ataxia and can be seen in the mouse mutant called Lurcher.

c. Molecular cell layer

A cell sparse region made up of neuronal processes. Their connections and glial cells stain light blue or red depending on which section you have. Granule cells have bifurcated processes that run perpendicular to the processes of Purkinje cells. Each granule cell contacts 100,000 – 200,000 Purkinje cells.

Make sure you can identify the following objects and regions in these histological preparations:

a. Granule cells/Granule cell layer
b. Purkinje cells/Purkinje cell layer
c. Molecular cell layer

IV. Cerebral Cortex Golgi Preparation
Slide 70829f (Cerebrum, Cat – Golgi Stained)

Note: The Golgi stain is an old, but poorly understood histological method. Pioneered by Golgi and used extensively by Cajal (neuroanatomy pioneers who won the Nobel prize for their work using the Golgi stain). It has the ability to produce a complete stain of a limited number of neurons. Those neurons that take up the stain will do so throughout the entirety of the neuron (including all of its processes). The result is the preservation of the morphology of a single neuron without the interference of neighboring neurons also being stained. This is a great method for studying the morphology of different types of neurons.

1. Look at a Golgi stain of the cerebral cortex under high magnification. Notice the thin, black, wispy lines running throughout the cortex. These are neuronal processes.
   a. How would you compare the complexity of the cerebral cortex to the cerebellar cortex?
   Depending on the tissue preparation you have, it may be difficult to observe a single neuron in isolation of others in the cerebral cortex. In fact, some Golgi preparations can highlight the large complexity of intertwining neuronal processes in the cerebral cortex. The complexity of the cerebral cortex is in stark contrast to the relative simplicity of the cerebellar cortex.
   b. Attempt to identify and distinguish axons from dendrites. How would you explain the difference to your lab partner if he or she were struggling to distinguish between them?
   If you are able to isolate a single neuron, it will have one axon that extends a thin process, usually from one pole of the neuron. The neuron will likely have multiple dendrites that extend from the other pole and arborize in a fashion consistent with the neuron type. When you observe cortical neurons, you will see many axons that extend towards the deep or subcortical layers.
   c. Can you see why dendrites are said to arborize? What does that mean?
   Many neurons have dendritic processes that look tree-like (i.e., like the branches and leaves of a tree that emanate or arborize from the main trunk.

V. Horizontal Section of Mouse Brain

Slide Ma521e (Brain of Mouse)

1. Start with low power magnification. Observe the general organization of the brain.
2. Identify the following structures or regions:
   a. Anterior aspect of the brain and olfactory bulb
   It may be easy to note the position of the cerebellum first and then the olfactory bulb and frontal cortex will be on the opposite end of the tissue.
   b. Posterior aspect of the brain and cerebellum. View the cerebellum. Attempt to identify the different layers. Notice the faintly blue stained areas in the white matter of the cerebellum. What are these structures? What is the functional significance of these structures?
   These are the deep cerebellar nuclei. On each side of the cerebellum are four nuclei, which receive modified sensory feedback and project to premotor areas to fine-tune motor programs.
   c. Cerebral cortex. The cerebral cortex is a six-layered structure. Describe the basic inputs/outputs that distinguish the different layers of the cortex.
   The individual layers will be hard to make out, but you should be able to see the cell-sparse Layer I that feeds into the more populated Layers II and III. Layers I-III are the main targets of fibers from the contralateral hemisphere (via the corpus callosum). Layer III also sends many projections to subcortical areas. Layer IV receives many fibers from the ipsalateral cortex as well as the majority of the thalamocortical afferents (fibers coming from the thalamus). Layer V is a primary site for motor efferents (output fibers) and is expanded in the frontal cortical areas. Layer VI is the major source of efferents to the thalamus, which produces a very precise reciprocal connection between the thalamus and cortex. Although not visible, the cortex is organized into functional columns that extend throughout the six-layered structure. The columnar organization is thought to help establish specialized modules of information processing with neighboring modules serving similar, but slightly different functions.
   Instructors Note: The pioneering work of Hubel and Wiesel might be discussed here, highlighting the functions of visual cortical cells.
   d. Hippocampus (look for the sea horse). What is the functional significance of this region of the brain? Describe how the adult neurogenesis that occurs in the hippocampus might be related to its function.
   The granule cells of the hippocampal formation look like two opposing C's. One C is part of the hippocampus proper (the CA1-CA3 fields), whereas the smaller C is part of the dentate gyrus. The hippocampus is an important limbic structure for memory. It is also a region that engages in continuous neurogenesis throughout adulthood. The new neurons are produced in the subgranular zone of the dentate gyrus and migrate a short distance where they are incorporated into functional hippocampal circuits. These new neurons are thought to be a mechanism whereby new memories and learning are accomplished via the new connections formed by these new neurons (in addition to other forms of synaptic plasticity).

VI. The Retina (V & C, pp. 63-65)

Slide 70713f (Retina from Human Eye)

Slide 70722f (Entrance of Optic Nerve in the Retina)

1. Each of these slides shows a cross section of the neural part of the back of the eye called the retina. The retina is neural tissue. In fact, it develops from an outcropping of the same tissue that forms the rest of the brain. The retina is a multi-layered structure.
    a. The most populated layer contains the photoreceptors that transduce light into neural impulses.
    b. The other layers contain processing cells and output cells (ganglion cells).
2. The axons of the ganglion cells form the optic nerve. They send information from the eye to the brain. The retina appears to have a backwards organization. Light must pass through all of the layers of the retina before reaching the photoreceptors. Once transduced, this information is sent back through the other layers to the ganglion cells on the way to the brain. What advantage does this type of organization afford the photoreceptors?

Note the backward orientation of the retina. The light must pass through all successive layers before reaching the photoreceptors. This means that the features of the retina must remain translucent in order to maintain the integrity of the photons entering the eye. This inside out organization becomes most problematic at the optic nerves. The optic nerves are composed of ganglion cell axons that are leaving the retina and heading for the rest of the brain. These fibers must pass through the entire retina. Therefore, the underlying layers of the retina are absent in this region (including the photoreceptors), which produces a blind spot. The blind spot is normally not noticed because we rely on binocular vision and we are capable of "filling in" the missing details with data from the other eye. Why are the photoreceptors in the deepest layer of the retina? The answer likely has to do with the nature of the work done by the photoreceptors. They receive energy in the form of photons and harness this energy to drive molecular reactions that result in ion channel gating and membrane potential alterations (i.e., visual transduction). The photoreceptors are very busy and receive much energy, whose heat must be dissipated. The supporting membranes, including the retinal pigmented epithelium (RPE) and choroid, on the opposing side of the photoreceptors, provide nutrients, remove wastes and provide a rich capillary plexus capable of acting as a radiator. Diseases or trauma that target the supporting membranes of the eye result in photoreceptor degeneration and varying degrees of blindness. In addition, the photoreceptor's outer segments disks have a short lifespan of about 12 days and must be removed, destroyed through phagocytosis, and renewed. The RPE is involved in the removal and phagocytosis of the outer segment disks. It also plays a crucial role in the retinal cycle where it helps in maintaining light sensitivity of the photoreceptors by aiding in the conversion of all-trans retinal back to 11-cis retinal.

3. Identify the following structures and describe the function of each:
    a. The three main layers of the retina

    The photoreceptor layer has both inner parts (where visual transduction takes place) and outer parts (where the cell bodies of the photoreceptors are located). The bipolar layer is the next superficial layer of cell bodies (mostly composed of bipolar cells). Actually, other layers on either side contain the synaptic connections of the various neuronal types to form a functional circuitry. The ganglion cell layer is relatively cell sparse compared to the other layers below, due to the convergence of the neural circuit.

b. The photoreceptors
Located in the most posterior aspects of the retina, the photoreceptors transduce light information by selectively absorbing light waves, which gate ion channels. The change in ion flow when light is present provides an electrical signal that is interpreted by structures distributed throughout the retina and visual pathway.
c. The optic nerve
Notice how the axons of the ganglion cells converge into the optic nerve. The optic nerve carries signals from the retina to the rest of the brain.
d. Retinal pigmented epithelium (RPE)
This structure opposes the photoreceptor layer, but is deeper than it. It is pigmented and usually stains a dark color. Other supportive structures such as the choroid may also be seen. As mentioned above, the RPE supports the photoreceptors.

VII. The Tongue
Slide 70701e (Tongue of Rabbit)

1. Tongue – notice the numerous papillae (like little mountains with valleys in between them).
2. In the valleys are small, rounded, clear objects. These organizations of cells are taste buds. What type of information is transduced by taste buds? In addition to the traditional taste buds, recent evidence supports the existence of two additional taste buds. What type of taste information do these buds convey? Taste is only one component of flavor. What is the other?

The taste buds contain receptor cells that transduce the chemicals in food into neural impulses. Along with odorant receptors, this information combines in the brain to produce flavor perception. The majority of, but not all, taste buds are located on the tongue. In addition to the traditional tastes of salt, sour, bitter and sweet, the taste buds also convey information about Umami or savory, and some researchers argue that there are mechanisms for conveying taste information about fatty substances. Umami is also described as a "meaty" taste and is activated by glutamate found in some foods such as the additive MSG, soy sauce, ketchup, some cheeses. The receptors for salt and sour are ionotropic, whereas the others (sweet, bitter, and umami) are metabotropic (g-protein coupled).

References

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Winkler, I., Cowan, R., & Paradiso, R. (Producers), & Winkler, I. (Director). (1999). *At first sight* [Motion picture]. United States: Metro-Goldwyn-Mayer.

C. Assignment 2: Neurotoxins

1. Research and describe how the tetraodon pufferfish defends itself. Use your new knowledge of neurophysiology to better explain the phenomenon. Additionally, describe the desired effect of this gourmet meal in Fugu restaurants and the physiological explanation for the effect.

2. Research and describe a different neurotoxin that is produced by another species (e.g., spider, snake) as a weapon or defense mechanism. Describe its physiological mode of action (that is, make sure you come up with a unique example that is not described in your text and make use of your new knowledge of neural communication in your answer).

To thoroughly complete this assignment, you will need to be able to describe neural communication and how these organisms target this process.

Assignment 2 Answer Key

1. The pufferfish, as well as other fish from the order Tetraodontiformes and several other species of animals, produces the tetrodotoxin that is found throughout its organs and skin. The tetrodotoxin works by binding an extracellular site on the pore of the voltage-gated sodium channel, which blocks this channel from functioning. The toxin binds to the tetrodotoxin-sensitive voltage-gated sodium channels found all over the body (especially in neural tissue) and not to the tetrodotoxin-resistant channels found primarily in cardiac tissue.

Antagonizing the voltage-gated sodium channels results in an inability to generate an action potential (AP). APs are generated when sufficient depolarization events (excitatory post synaptic potentials) bring the membrane potential to threshold (around -70 mV depending on the type of neuron). The threshold is established by the voltage sensitivity of the voltage-gated sodium channels. At threshold, these channels are gated, and sodium rushes into the cell due to the electrostatic and concentration gradients established by the sodium/potassium pump. Once sodium begins to enter the cell a series of events begin that will result in the characteristic membrane potential changes called the AP. For example, voltage and gradient changes generated by sodium influx will gate voltage-gated potassium channels.

The toxicity of the tetrodotoxin comes from its inhibition of myocyte contraction. Myocytes contract when acetylcholine from motoneurons binds to receptors on the myocytes. Inhibition of the AP will prevent ACh from being released and will result in paralysis, with heart and respiratory failure.

In small concentrations the tetrodotoxin will produce partial anesthesia as it prohibits the propagation of sensory signals. Partial anesthesia (i.e., a numbing feeling) is the goal of the specially trained and licensed Fugu chefs of Japan where the pufferfish (Fugu) is considered a delicacy.

2. Students have a wide range of choices for completing this portion of the assignment. Students should demonstrate an understanding of the neurophysiological consequences of the toxin they choose to report. For an excellent review of many types of neurotoxins and their mechanisms of action, see http://faculty.washington.edu/chudler/toxin1.html.

D. Assignment 3: Neurophysiology

Ethyl alcohol is found in beer, wine, distillates, etc. It is classified as a Central Nervous System (CNS) depressant. Suppose I tell you that alcohol works on the CNS by facilitating chloride channel gating mechanisms.

1. Using your newfound knowledge of neurophysiology, explain how this mechanism of action leads to its CNS depressant effect. In other words, describe the membrane potential changes that will take place, why they take place, and what result they will have.

2. Provide a possible explanation for why alcohol has biphasic effects (small concentrations produce relaxation and cheerfulness, but large doses produce slurred speech, coordination problems, memory impairments, etc.).

Assignment 3 Answer Key

1. Although it is not clearly understood where alcohol binds on the GABAa receptor, its presence facilitates the activity of GABA. It is considered an allosteric modulator because it binds to a site other than the primary receptor site to influence the conformation of the channel pore. In other words, in the presence of ethanol, GABA binding produces a more potent effect than would occur in its absence. Because GABA binding to the GABAa receptor gates a pore for chloride and because chloride will flow into the cell based on its electrochemical gradient, ethanol allows more Cl- to flow into the cell than does GABA alone. Ethanol is thought to facilitate GABA by holding the pore open wider and for a longer period of time. The net result of ethanol is to hyperpolarize the neuronal membrane (inhibitory postsynaptic potential), which will bring the membrane potential farther below threshold levels. This means that the neuron becomes less likely to produce an action potential. A general reduction of CNS activity is a hallmark of a CNS depressant.

2. First, in small concentrations, ethanol may produce disinhibition. In other words, tonic inhibition present throughout the neural circuits of the brain may themselves be inhibited. Inhibition of inhibitory synapses produces disinhibition. In small concentrations, ethanol affects fewer areas of the CNS, including the frontal cortex where impulse control may be affected (release of inhibitions). Additionally, ethanol is known to alter opioid peptide signaling (especially in the reward regions of the brain), which is involved in producing euphoria. As the dose of alcohol is increased, it begins to affect a larger proportion of the brain. Its eventual ability to depress brainstem activity, which controls many vital functions like heart rate and respiration, explains its lethal capabilities. In addition to the actions of ethanol on the GABA system, it also affects glutamate signaling by potentiating signaling through the NMDA receptor. The biphasic effects, therefore, might be explained by disinhibition, NMDA facilitation, and concentration dependent effects.

References

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E. Assignment 4: Prosopagnosia

Read the title story from Oliver Sacks' (1985) book *The Man Who Mistook His Wife for a Hat.* Dr. P. obviously had some serious problems, including a disconnection between sensation and perception. Answer the following questions:

1. Based on the information presented in the case study, where do you think Dr. P.'s brain damage was located (generally and specifically)? In localizing the damage, consider that Dr. P. was once able to recognize a student as follows: "That's Karl. I know his movements, his body movements."
2. What additional pieces of information led to your conclusion in question #1 (i.e., what symptoms did he display and what functioning did he maintain versus lose)?
3. Additionally, what role did nonvisual stimuli play in his functioning and what does this suggest about the cross-talk between sensory systems?
4. Why is multi-modal processing so important for our everyday functioning?

Assignment 4 Answer Key

1-2. Dr. P. did not have a problem with his eyes or his primary visual cortex. He was able to see features of the object, such as color, movement, and shape. However, he was not able to combine these features together into a meaningful, whole perception. Such combination is the job of the visual association cortices. The visual system works by breaking down the visual scene into its constituent parts. Each part is analyzed along parallel pathways with each stop resulting in more complex processing of the visual scene (i.e., hierarchical processing). Each visual modality provides important information about the visual scene that then must be bound together into a meaningful whole. Exactly how this binding occurs is at the very heart of the conscious experience and is beyond the scope of this discussion, but it does make for a nice tangential classroom discussion. Many of the modality-specific association cortices are located in the occipital lobe; in contrast, the multi-modality cortices are located at and around the intersections of the occipital lobe with the temporal and parietal lobes. The temporal and parietal lobes house two distinct multi-modal, parallel pathways that originate within the retina. The dorsal pathway originates from the rods. The dorsal system is specialized for detecting movement and has been given the moniker of the "Where Pathway." Damage to the dorsal pathway can result in akinetopsia, which is a selective loss of motion perception. Those with this condition perceive their visual scene as if viewing it in a dark room with a strobe light. A person approaching them might be seen at a distance one instant and then suddenly appears to be next to them. The ventral pathway originates from the cone system and appears to be specialized for determining form and function. This is the so called "What Pathway." Identifying an object requires an analysis of form and color as well as an ability to access the object in memory and report the identification process. This analysis is a multi-sensory, multi-modal process. Any one of these processes can be affected, resulting in various forms of aphasias and agnosias. For example, damage to V4 may result in achromatopsia or color blindness, whereas damage to the superior temporal lobes may result in different forms of agnosias, such as prosopagnosia or face blindness.

Dr. P. clearly had a form of prosopagnosia in that he lost the ability to recognize faces, even for people very familiar to him like his family. He was "Mr. Magoo-like" in that he often confused inanimate objects for people and attempted to strike up conversations with them. He even mistook his wife for a hat. Dr. P. could recognize some people, but only if they had a unique or exaggerated feature. For example, he identified his brother by his square jaw and Albert Einstein by his crazy hair. This suggests that his ability to perceive facial features was intact. Perhaps if the feature was distinct, it alone was sufficient to elicit the memory of that individual and, hence, his or her identification. These data suggest that Dr. P.'s problem was restricted to higher visual association cortices. Dr. P.'s recognition of Karl based on his body movement suggests that Dr. P.'s dorsal stream was intact. Finally, when asked to imagine that he were walking through his home town's square and to report the buildings he could see, Dr. P. omitted all of the buildings on his right side. When asked to imagine that he was entering the square from the opposite direction, Dr. P. now noted those buildings that were previously omitted, but omitted those that were previously noted (these buildings were now located on his right). His damage must have been confined to the left ventral pathway. Dr. Sacks suggests that at least portions of Dr. P.'s temporal lobes were intact due to his continued musical abilities, but that the interface of the temporal, parietal and occipital lobes was damaged.

Studies published since Dr. Sacks wrote of Dr. P. have identified a region of the superior temporal gyrus called the fusiform face area thought to be involved in face perception and which when damaged can lead to prosopagnosia. It is interesting that we might have specialized areas in the brain for processing data about faces and for recognizing other individuals. Consider the evolutionary importance of such an ability. Still other studies have suggested that the fusiform face area is not merely devoted to face processing, but might be used to analyze any number of complex, multi-featured stimuli (even completely made-up stimuli like Greebles). Additionally, other adjacent areas in the ventral pathway may serve the very same function of combining features into complex whole perceptions for different types of stimuli. Only rarely is brain damage confined to a small brain locus. In Dr. P.'s case, he had difficulty identifying many types of complex objects. A final note is that Dr. P. did not appear to be consciously aware of his condition.

3-4. Dr. P. was asked to identify a glove and a rose. He identified their features flawlessly (e.g., "About six inches in length. A convoluted red form with a linear green attachment," p. 13), but had extreme difficulty identifying the objects unless further prompted. For example, when Dr. Sacks asked him to smell the rose he replied, "Beautiful! An early rose. What a heavenly smell!" (p. 14). It seems that Dr. P. was able to use a different sensory modality to elicit the memory of the rose and correctly identify it. In reality, we rarely rely on a single sensory modality to identify or interact with our world. However, when missing or ambiguous information is presented through one modality, we often compensate by relying on a nontraditional form of processing (e.g., we attempt to understand people with a thick accent by listening *and* watching their lips). Therefore, memories are probably stored as an amalgamation of sensory data. As such, Dr. P. was likely able to access some memory stores through the back door. Oliver Sacks writes of another patient named Virgil with visual deficits and made popular by Val Kilmer's depiction of him in the movie *At First Sight* (1999). Virgil developed cataracts as a young child and was virtually blind soon after. He underwent surgery to remove the cataracts as an adult only to be very confused by his visual world. His brain had not developed to understand movement and form and, in many ways, he had missed his window of opportunity for understanding these things. He often performed much like Dr. P. in that Virgil became interested in the features of the visual world, but had difficulty with complex, whole perceptions. Virgil had learned about his world by relying on his other sensory modalities. Therefore, he probably had developed very different memories of everyday objects. This is highlighted by the fact that when Virgil became overly confused by his visual world, he would resort to closing his eyes and using his other senses (e.g., feeling an object) to develop an understanding of what he was “seeing.”

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F. Assignment 5: Mirror Neurons

Mirror neurons have become all the rage in the neurosciences. Scientists speculate about their role in the evolutionary emergence and development of language as well as the development of a theory of mind and autism. They have also been speculated to be involved in social learning and empathy construction.

What are mirror neurons? What do they do? Where are they located? Make an argument for mirror neuron involvement in each of the above instances.

Assignment 5 Answer Key

In 1996 a group of Italian researchers described a subset of neurons found in Area F5 in the frontal lobe (premotor cortex) of the monkey brain that were responsive when a specific action was performed by the monkey and when the monkey observed the same action being performed by another (Rizolatti, Fadiga, Gallese, & Fogassi, 1996). These neurons have been given the name mirror neurons because they mimic actions that are merely observed. The premotor cortex is involved in the production of motor programs. It projects to the primary motor cortex, which commands the muscle groups needed to complete action plans produced in the motor association cortices.

Additional neurons with mirror properties have more recently been found in the inferior parietal lobe (Fogassi et al., 2005), a brain region known to integrate multi-modal sensory information. Neurons in the inferior parietal lobe (IPL) receive a strong connection from the superior temporal lobe (STS; a visual association cortical area that is especially activated by biological motion) and send reciprocal projections to the premotor cortex. Of particular interest is a study by Fogassi et al. (2005) in which IPL mirror neurons in the macaque brain were recorded when (a) the monkey performed an action; (b) the monkey observed the same action being performed with intent; and (c) the monkey observed the same action without intent. Some mirror neurons were activated when the action (grasping an apple) was performed or observed by the monkey, whereas the activation of other neurons depended on the intentions of the monkey performing the observed action (placing the apple in a cup or bringing the apple to the mouth). These neurons may be predicting the goal of the observed biological movement (moving an apple or moving an apple to eat it). Iacobini et al. (2005) reported similar results in human subjects. Presuming that these neuronal circuits can be altered due to the observed experience (e.g., via long-term potentiation), the mirror neuron system may provide a physiological explanation for very basic forms of social (imitative) learning.

Can the mirror neuron system model more complex forms of social learning? It is very difficult to apply behaviorist principles in a social context, especially given that much learning does not necessitate that the learner directly receives the stimuli or consequences that are being associated during classical and operant conditioning. For example, if I watch my brother get punished for sassing my parents, I can learn that sassing produces bad consequences even though I did not perform the behavior nor did I directly experience the consequences of that behavior. Perhaps the mirror neuron system allows for these indirect experiences to activate neural circuits in a similar fashion as though the observer had experienced them himself or herself. If these neural circuits undergo plasticity to reflect these experiences, we can model social learning in a similar fashion as we can model direct behavioral learning. Implicit in the set of assumptions above is the observer's ability to analyze the valence of the consequences the model experiences as a result of his or her behavior.

Recently, subsets of neurons with mirror qualities have been found in the insular cortex. Although the insular cortex has been neglected in the neurosciences for many decades, it is thought to play a role in integrating the physiological responses of the body to external stimuli and to help generate a subjective feeling to these responses. It is a component of the limbic system and receives strong connections from other emotive areas, such as the amygdala. The insular cortex is strongly activated by all basic emotions, including fear, pain, anger, disgust, and happiness and it is reciprocally connected to the other major components of the mirror system (i.e., the IPL, STS, and IFL).

In 2003, Wicker et al. gave participants a disgusting odor to smell while their brain activity was being recorded. As expected, the insular cortex was strongly activated by the smell. The participants in this study were also shown pictures of other people displaying an emotional reaction. The participants correctly identified that they were observing the display of disgust, and a response of their insular cortices supported this emotional assessment. Likewise, lesions in the insular cortex abolish a person's ability to judge facial expressions for emotional content. It appears as though this region is activated both by the person's own emotional responses as well as when the person observes others experiencing the same emotions. Not only does this system allow us to understand the consequences of someone else's actions, it may provide a substrate for understanding what someone else is feeling or thinking. The expansion of the mirror neuron system might also be used to explain empathy and the development of a theory of mind, which are key to understanding the human experience. Furthermore, Ramachandran (2000) suggests that the ability to mimic these uniquely human qualities through social learning is key to the development of culture.

Although autism is a complicated disorder with an unknown etiology, evidence suggests that autistics display a reduced mirror neuron response, specifically to the intent of others' behaviors (Gallese, 2006). Autism is usually associated with abnormal social abilities that might result from a lessened ability to understand what others are feeling and thinking. The reported reduction in mirror neuron response might contribute to the abnormal development of a theory of mind and one of the primary symptoms experienced by autistics.

Given that one theory of language development presumes language to have evolved from a simple system of gestures (i.e., biological movements; Skoyles, 2000), the evolution of an expanded set of mirror neurons may be a means by which humans expanded their communicative abilities beyond those of their ancestors (Ramachandran, 2000).

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G. Assignment 6: Cranial Nerve Zero

1. There are many examples of mammalian pheromone effects on sexual reproduction. Describe the following examples: Whitten effect, Vandenberg effect, Lee-Boot effect, Bruce effect, and Coolidge effect.
2. Read the article referenced below concerning the terminal nerve. Are humans capable of using pheromone signaling too? Do some academic internet research and look for supporting evidence and counterevidence. Summarize this evidence and your viewpoint.

Fields, D. F. (2007). Sex and the secret nerve. *Scientific American Mind, 18*(1), 21-27.

Assignment 6 Answer Key

1. Whitten effect: Male pheromones induce estrus, sexual receptivity and fertility in females.

Vandenberg effect: Male pheromones accelerate puberty in females.

Lee-Boot effect: Female pheromones suppress estrus of other females and delay puberty of younger females.

Bruce effect: Male pheromones from a new potential mate cause abortion of a newly fertilized egg by preventing implantation. The female returns to estrus.

Coolidge effect: A refractory period from sexual activity due to a loss of interest in sex after mating. Pheromones from a new mate renews sexual interest.

2. Students might cite the McClintock effect that concerns the ability of pheromones to synchronize the menstrual cycle (McClintock, 1984). Students might also cite studies that suggest human mate selection involves an analysis of the potential mate's Major Histocompatability Complex (MHC), which the immune system uses to detect self from non-self. The theory holds that humans choose mates with compatible immune systems (i.e., mates who do not share their MHCs and are, therefore, not closely related to themselves; Wedekind Seebeck, Bettens, & Paepke, 1995). Still other research suggests that homosexual and heterosexual men respond differently to odors and that homosexual men are sexually aroused by odors in a fashion that is more similar to heterosexual women than to heterosexual men (Savic, Berglund, & Lindstrom, 2005). Recent studies show humans have orthologs to mouse trace amine-associated receptors that are responsive to the volatile compounds found in mouse urine (Liberles & Buck, 2006). Finally, a chemical found in male sweat called androstadienone induces changes in female hormone levels (increased cortisol levels) and causes other physiological (blood pressure, heart rate, and breathing) and psychological (elevated mood and increased sexual arousal) changes (Wyart et al., 2007).

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H. Assignment 7: Sexual Orientation

Describe the current state of research on the possible biological basis of sexual orientation. In particular, how might neurobiological mechanisms be used to help explain male preferences for male versus female partners or female preferences for female versus male partners? Be sure to include information about organizational and activational hormonal effects, and sexually dimorphic nuclei in your explanation. Be sure to provide a critique of the research you reference.

Assignment 7 Answer Key:

A wealth of data supporting a biological basis for sexual orientations exists and is highlighted in the Carlson text (Chapter 10: Reproductive Behavior; pp. 342-362). Students should look beyond the text and attempt to support their viewpoint via peer-reviewed sources and academic internet research. An important component of this assignment is that students should critique the sources they use to support their viewpoint. Common student errors might include (a) inappropriately reporting correlation as causation, and (b) failing to note a lack of reliability across a particular research topic. Students should be graded on the quality of their answer and not the direction of their conclusion. Also, a thorough discussion ought to follow this assignment.

Students should describe the difference between organizational and activational hormonal effects in sexual development. They should draw several links to hormonal responses and sexual behaviors in the context of sexual dimorphism. Students should also describe heritable events and environmental influences that might lead to altered organizational effects and, therefore, altered activational effects and dimorphism. They might draw inferences as to how these alterations can influence sexual orientation.

I. Assignment 8: Hypothalamic Neurogenesis

Does adult neurogenesis have a possible role in controlling our appetitive drives?

Read the Kokoeva, Yin, and Flier (2005) article referenced below. Use the following background information and discussions from class to answer the questions provided.

Kokoeva et al.'s report is truly an exciting paper on many levels:

1. If their results prove to be replicable, this is the first demonstration of a physiological effect from the addition of new neurons in the adult brain and their role in pathophysiology.
2. It is another piece in the puzzle in our attempts to understand how to treat a major risk factor for any number of health problems.

Growth factors are thought to control a number of developmentally related processes in the brain including neuron growth, differentiation, migration, and survival, to name a few. Many growth factors have been investigated as treatments for neurological disorders. Ciliary neurotrophic factor (CNTF) has long been recognized as a growth factor capable of keeping neurons alive, and it promotes their differentiation. It was tested in clinical trials as a treatment for Amyotrophic Lateral Sclerosis (ALS or Lou Gehrig's disease) that results in the death of motoneurons. Strangely, the patients lost their appetites and a great deal of weight. More recent studies have shown that CNTF could do the same thing in virtually all experimental mouse models of obesity and led to the development of Axokine as a successful, long-lasting treatment for obesity. But what is CNTF doing? The answer may be of some surprise.

A) In your own words, summarize the major findings of this paper.

B) Explain the rationale for the following experiments in this study and how the results from these studies support the authors' conclusions:

1. BrdU labeling
2. Hu and TUJ1 immunostaining
3. Ara-C treatment
4. pSTAT3 immunostaining
5. ob/ob mice

Kokoeva, M. V., Yin, H., & Flier, J. S. (2005, October 28). Neurogenesis in the hypothalamus of adult mice: Potential role in energy balance. *Science, 310,* 679-683.

Assignment 8 Answer Key:

Traditional dogma in the neurosciences dictates that after a certain point in development the production of neurons ceases in the CNS. Although first suggested long ago and oft debated in past decades, it is now appreciated that new neurons do continue to be produced in discrete regions of the adult human brain. The first identified and most prolific regions include the forebrain adult subventricular zone (aSVZ) and the subgranular zone (SGZ) in the dentate gyrus. The proliferative capacity of these regions can be regulated by both endogenous (genetic profile) and exogenous factors (stress, exercise, circulating cytokines, and growth factors, etc.). It is exciting to think that the new neurons being produced in each region are emanating from a stem cell or at least a cell with stem-like properties (i.e., self-renewing and pluri or multipotent). The ability to manipulate such a cell creates a host of potential treatment strategies for neurological disorders, and adult neurogenesis will likely raise many questions about stem cell research that could be addressed in class.

What is the function of these new neurons and why are they being produced in the first place? The aSZV is likely the developmental remnant of a major neurogenic region, which produces the majority of cortical neurons. These neurons are produced in close proximity to the ventricle and migrate to their final destination in the cerebral cortex. Waves of migration along radial glia and migratory cues probably contribute to the laminar development of the cortex. This region progressively self-depletes as development progresses. In the adult brain, neurons and glia cells are produced in the aSVZ in the anterior portions of ventral aspects of the lateral ventricles. These new cells migrate along the well-defined rostral migratory stream (RMS) toward the olfactory bulb. The RMS is bounded by special glial tubes and contains several developmentally conserved circulating factors aiding in the migratory process. The new neurons that are produced will differentiate en route into olfactory bulb interneurons. The new neurons in the dentate gyrus are produced in the region directly under the granular layer. They differentiate into granule cells and migrate a short distance into the granular layer, where they produce functional connections with other dentate gyrus cells. It is speculated that these new neurons are involved in plastic changes associated with learning and memory and provide a model whereby learned events can be stored in the CNS as altered connections between neural circuits. The hippocampal formation is known to be involved in certain types of learning and memory (e.g., explicit and spatial/relational memories). The involvement of adult neurogenesis in learning and memory will likely raise many questions that could be addressed in class.

Are there other neurogenic regions of the adult brain and if so what are their functions and potential for therapeutic treatments? The article referenced above suggests that other brain ventricular-associated structures may have neurogenic potential with functional significance. The article highlights a number of experimental techniques that elucidate the functional significance of a diencephalon neurogenic region. Student should explain the rationale for the use of these strategies, which include the use of immunohistochemistry to identify mitotic cells (BrdU labeling), the use of immunohistochemistry to identify neurons (HU/TUJ1 labeling), the consequences of prohibiting protein production (Ara-C treatment) and identifying (pSTAT) and manipulating (ob/ob) hypothalamic signal transduction mechanisms. By delving into a complicated primary research article, students learn how to dissect it and interpret its results.

J. Assignment 9: Addiction

Some people argue that addiction is an aberrant form of learning, involving motivated behaviors and hedonic responses. In fact, anatomical and biochemical changes like those that occur during other learning paradigms have been noted. Still others support this view by suggesting that both classical conditioning and operant conditioning both maintain drug use and abuse and initiate it.

1. Describe how classical conditioning might establish the formation of drug cues and the development of cravings that are so troublesome to abstinent addicts and that are often the root causes of relapse.
2. Describe how operant conditioning might be involved in the initiation of drug use and the continuation of use even after tolerance to the euphoric effects of the drug has occurred.
3. Finally, speculate as to the neurological bases of these learned events.

Assignment 9 Answer Key:

In classical conditioning, learners associate two stimuli such that the presentation of one stimulus produces the expectation of the other. In the classical conditioning paradigm, an unconditioned stimulus (UCS) produces an unconditioned response (UCR). No learning needs to take place for this association to occur. Pavlov did not need to teach his dogs to salivate when food was present (this is an innate response). However, the introduction of a neutral stimulus (e.g., the sound of a bell) did not produce a salivary response until it was repetitively paired with the UCS. The new salivary response to the bell (now a conditioned stimulus [CS]) is considered a conditioned response (CR). An association between the food and the bell was learned, which produced a measurable response.

Simple forms of learning, such as classical conditioning, can be modeled using Hebbian principles. Convergent synapses that are simultaneously and repetitively stimulated can induce short-term and long-term plasticity in the connections between neurons. One such plastic change involves activation of NMDA receptors and long-term potentiation (LTP) which is described in detail in the Carlson text. Many drugs of abuse induce activity in and plastic changes to many brain regions including the mesocorticolimbic dopamine reward pathway originating in the ventral tegmental area and projecting to the nucleus accumbens in the limbic system and the prefrontal cortex. Among other things, the activation of this system is thought to underlie the euphoria or "high" associated with drug use. Drugs of abuse are often used in a ritualistic way. For example, a drug user may use with certain people, in a certain place, during a certain time of day, etc. These rituals provide ample opportunities for neutral stimuli (sight of a needle, exchange of money, etc.) to become paired with the drug. If the drug is an UCS that produces a series of UCRs (including activation of certain brain circuits), it stands to reason that neutral stimuli can become CSs that produce CRs. According to Hebbian principles, the CS might elicit activation of brain circuits in a similar fashion as the drug itself (UCS). This activation might then signal to other neural circuits that the drug will follow. Recent reports show that lesions in the insular cortex can abolish an addiction to nicotine. If we speculate that the insular cortex is involved in integrating the physiological responses of the body to the drug exposure and helps to generate a subjective feeling towards these responses and if we speculate that over time classical conditioning can elicit similar responses in the insular cortex to originally neutral, but now drug-related stimuli, then we might see how the insular cortex activation by drug-cues could elicit strong cravings for that drug. In other words, in the presence of classically conditioned drug cues, the brain may prepare for and expect the drug to follow. When it does not, we may experience a craving. Given that learning is defined as a relatively permanent change in behavior due to experience and that plastic brain changes that might underlie learned events can be maintained for extended periods of time, the induction of cravings as described above can occur even years after drug abstinence.

In operant conditioning, an association between a behavior/stimulus and its consequences is learned. If the consequence increases the likelihood of the behavior occurring again in the future, reinforcement has occurred. The valence of the reinforcer can be positive or negative. A positive reinforcer increases the likelihood of the behavior because the consequence is something pleasant. Most drugs of abuse produce euphoric feelings and, therefore, the behavior (drug use) will likely occur again in the future. Many drugs of abuse are also negative reinforcers because their use removes something unpleasant. For example, alcohol use may be euphoric (positive reinforcement), but it can also remove inhibitions, reduce tension/stress, as so forth (negative reinforcement). Other drugs may remove pain (opiates) or anxiety (anxiolytics). Reinforcement might help to explain why a person initiates drug use and continues to use it. However, for many drugs of abuse, the user rapidly develops a tolerance to the desired drug effects described above including euphoria. Tolerance results from physiological adaptations to the presence of the drug and is a form of plasticity. Withdrawal results from drug abstinence once tolerance has developed. Withdrawal symptoms are generally experienced as the opposite effects produced by the drug. If a stimulant drug causes euphoria, enhanced concentration, and increased energy, the withdrawal symptoms would include dysphoria, trouble concentrating and sleepiness. Withdrawal symptoms can be quite severe, painful, and life-threatening. According to operant conditioning principles, a user may continue to use drugs to avoid the symptoms associated with withdrawal (negative reinforcement) even when the desired effects of the drug lessen due to tolerance. Plastic changes in specific brain pathways might underlie these forms of learning as well and are highlighted in the Carlson text.

Carlson, N. R. (2007). *Physiology of behavior* (9th ed., pp. 615-641; 431-479). Boston: Allyn and Bacon.

K. Assignment 10: Movement Disorders

Parkinson's Disease (PD) and Huntington's Disease (HD) both produce motor impairments by disrupting brain circuitry involved in movement control. Describe how each of these disorders produces its motor symptoms by describing (a) the region of the brain that degenerates and (b) the role of this brain region in basal ganglia function.

Using what you have learned about neurotransmitter signaling, research and explain a pharmacological treatment strategy for Huntington's Chorea. Be sure to explain how the drug is targeting the dysfunctional basal ganglia circuitry and its mechanism of action (e.g., direct or indirect agonist or antagonist). A complete answer will fully elucidate the treatment strategy being targeted with the use of the drug.

Answer Key

The control of voluntary movement by the nigrostriatal system is complicated and students will often gloss over the details of such neurocircuitry. This assignment provides an opportunity to explore the neural circuits by examining Parkinson's disease, which results in a paucity of voluntary movement due to the degeneration of neurons in the substantia nigra pars compacta, and Huntington's Chorea, which results in an exaggeration of movements due to the degeneration of excitatory neurons in the striatum. Carlson (2007) should elucidate the pathways and how they are differentially altered by each disease process (i.e., hypoactivation of the motor cortex [PD] vs. hyperactivation [HD]). The student should demonstrate an understanding of disinhibition in these processes.

Academic internet research should provide a wealth of information concerning pharmacological treatments for HD. In general, a drug that mimics the activity of the neurotransmitter system it is targeting is considered an agonist. A drug that reduces or blocks the activity of this system is considered an antagonist. Of course, drugs can be agonists or antagonists by altering any of the steps in neurotransmission (e.g., neurotransmitter production, storage, release, receptor binding, and neurotransmitter clearance). Drugs with direct mechanisms of action will bind to the same receptor location as the neurotransmitter. If this drug activates the receptor in the same way as the neurotransmitter, it is considered a direct agonist. If the drug blocks the activity of the neurotransmitter, it is a direct antagonist. A drug that works elsewhere in the synapse is an indirect agonist or indirect antagonist. For example, PD patients may receive an amphetamine drug to treat their dopamine (DA) imbalance. Because amphetamines will cause an increase in the release of DA from postsynaptic terminals and a decrease in the removal of DA from the synapse, it is a DA agonist (i.e., it produces an increased activity in the DA system). However, because the mechanism of action of the amphetamine is not the postsynaptic DA receptor (it targets the intracellular and extracellular transporters as well as MAO, which is an enzyme that breaks down DA), it is an indirect agonist.

Carlson, N. R. (2007). *Physiology of behavior* (9th ed., pp. 110-113; 532-538). Boston: Allyn and Bacon.