

Name _____

(write your name on every sheet)

HST 131/Neuro 200
Exam III, Nov 23, 2005

There are 25 questions.

Point values for each are given.

100 points total.

1. List the four types of retinal neurons other than photoreceptor cells. List the layers of the retina where their processes receive input, in which their nuclei lie, and the region to which they project output: (8 points)

a)

b)

c)

d)

Answer:

Bipolar: Input: Outer Plexiform Layer (OPL). Cell Body: Inner Nuclear Layer (INL). Output: Inner Plexiform Layer (IPL)

Horizontal: Input: OPL. Cell Body: INL. Output: OPL.

Amacrine: Input: IPL. Cell Body: INL (some are displaced). Output: IPL.

Retinal Ganglion: Input: IPL. Cell Body: Ganglion Cell Layer. Output: to higher targets (LGN, SCN, Superior Colliculus, OPT, etc).

2. We have the capacity to focus our vision on objects both very near and very far. If you are looking at a distant object and then bring your eyes to focus on a nearby object, the eyes exhibit a predictable set of behaviors together called the “near response.” List the three main components of the near response and the function of each component of the response. (6 points)

1. convergence – point the eyes towards the near object of interest

2. accommodation – adjust the lens optics so that the nearby object is in focus on the retina

3. pupillary constriction – shrinking the pupil reduces spherical aberration, increases depth of field

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3. We learned that the majority of retinal ganglion cell responses can be grossly categorized as having either OFF or ON center responses when they decrease or increase spiking activity in response to light, respectively. For each cell type feeding into the two pathways, indicate whether the cell is depolarized or hyperpolarized by light. For each synapse, indicate whether the synapse is excitatory or inhibitory (circle the answer) (5 points).

	<u>ON center response</u>	<u>OFF center response</u>
Cone photoreceptor	depolarized <input type="checkbox"/> hyperpolarized	depolarized <input type="checkbox"/> hyperpolarized
Synapse	excitatory <input type="checkbox"/> inhibitory	<input type="checkbox"/> excitatory inhibitory
Bipolar cell	<input type="checkbox"/> depolarized hyperpolarized	depolarized <input type="checkbox"/> hyperpolarized
Synapse	<input type="checkbox"/> excitatory inhibitory	<input type="checkbox"/> excitatory inhibitory
Ganglion cell	<input type="checkbox"/> depolarized hyperpolarized	depolarized <input type="checkbox"/> hyperpolarized

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4a. (6 pts) What are the major molecular events in the olfactory sensory transduction cascade? Begin with the binding of odorant to receptor and end with depolarization of the olfactory receptor membrane.

4b. (2 pts) At which step(s) in this cascade does amplification occur?

Answer:

a. Odorant binds to receptor ==>receptor binds to Golf which dissociates in to alpha and beta-gamma subunits ==> alpha binds to and activates adenylate cyclase(AC) ==> AC converts ATP into cyclic AMP ==> cAMP binds and activates cyclic nucleotide-gated cation channel ==> inward current depolarizes olfactory neuron.

b. 1) The odorant receptor activates many G proteins.

2) Adenylate cyclase converts many molecules of ATP to cAMP.

5. Which cell types make afferent synapses onto the olfactory mitral cells? Specify cell type, neurotransmitter used, and histological region where synapses are formed. (6 points)

Cell type:

Region:

Transmitter:

(1)

(2)

(3)

Answer: (1) Olfactory Sensory Neuron, in the Glomeruli of the Olfactory Bulb, Glutamate; (2) Granule Cells, in the External Plexiform Layer of the Olfactory Bulb (or, outside of the glomeruli in the olfactory bulb), GABA (Extra credit for this being reciprocal); (3) Periglomerular cells, in the Glomeruli of the Olfactory Bulb, GABA (Extra credit for this being reciprocal).

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6. In class we visited with a patient suffering from retinitis pigmentosa. Answer the following basic questions about the disease.

- a. If you were to look at a cross-section of the retina, which cell types would you observe to be predominantly affected by the disease? (1 point)

rod photoreceptors

- b. What symptoms would you expect the patient to describe, and how would you expect those symptoms to evolve over the natural course of the illness? (3 points)

difficulties with night vision, difficulty with peripheral vision, often describe bumping into things or loss of coordination as it is difficult to notice such a slowly-progressing visual impairment

- c. In which gene are the majority of the causative mutations found? What is that gene product's normal function? (1 point)

rhodopsin

Higher Visual Processing/Cortical Visual Processing:

7. Name and describe three response properties that V1 neurons that are near each other are likely to share (3 points).

1. receptive field location – adjacent neurons are likely to respond to stimuli in nearby regions of space

2. orientation – adjacent neurons are likely to respond to the same or similar orientations of edges in their receptive fields

3. ocularity – responses of adjacent neurons are likely to be dominated by visual input from one eye

8. In the glabrous skin of your hand: (circle all that apply; 2 points)

- a. The most numerous mechanoreceptors are Merkel's disks
b. Meissner's corpuscles would be activated by a handshake
c. You can detect two moving ants separated by a distance of 7 millimeters
d. Pacinian corpuscles are not so important for fine discrimination

Answer: B, C, D

9. Pain pathways: Characterize **two** different peripheral **fiber** types that convey pain to the brain. How do differences in the structure of the pathways underlie differences in perception of pain? (4 points)

(1) A-delta fibers: Myelinated, thus fast (5-30m/s). Sensation onsets more rapidly than C fibers. Conveys pain from thermal and mechanical nociceptors.

(2) C fibers: Unmyelinated, and thus slower (<1m/s). Can convey pain from polymodal nociceptors.

(3) A-beta fibers: Large myelinated fibers with low input threshold from mechanoreceptors. Restricted RF and respond predominantly to non-noxious stimuli (thus, not pain and not as good an answer as (1) and (2)).

10. What is referred pain? Give an example of how the patient may describe referred pain. Explain what this means and suggest a possible mechanism. (3 points)

Referred pain is a condition in which pain or damage in a visceral organ is perceived as originating in the body wall or surface. This includes, for instance, the radiating pain in the left arm during a heart attack/myocardial infarction. One hypothesis: some of the target neurons (projection neurons) of the nociceptors in the spinal cord receive inputs from both visceral organs and skin; thus higher centers are unable to distinguish the source.

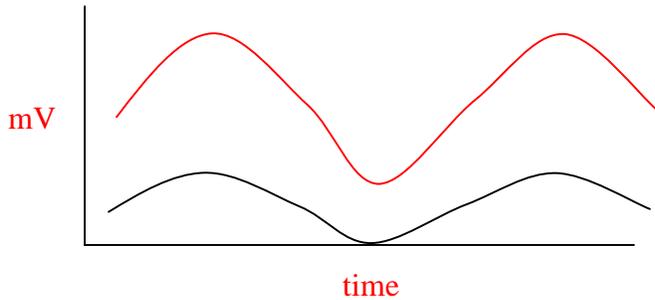
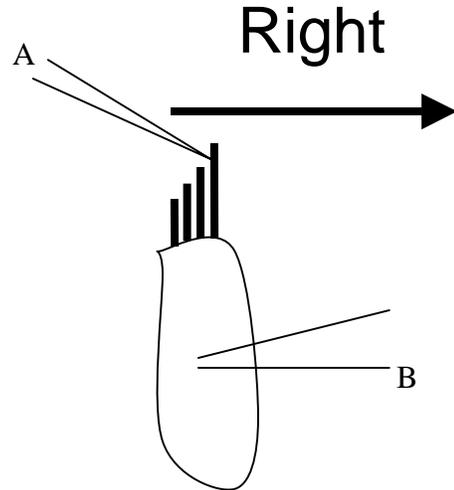
11. Which are true about hair cell adaptation? (2 points)

- a. Adaptation is important to increase the range of sensitivity of the cell
- b. Adaptation is mediated by a motor molecule of the actin family
- c. After adaptation a smaller movement of the hair bundle is needed to open 20% of the transduction channels than before adaptation.
- d. The tiplinks are not important for adaptation

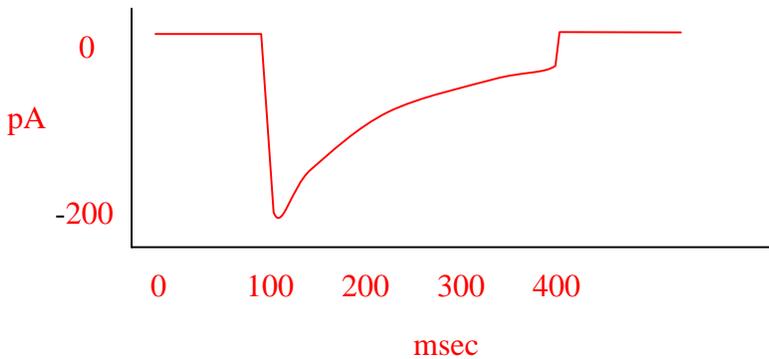
Answer: A

12. You're recording in whole cell mode (pipette B) from a hair cell in a utricle prep, and you're trying to understand how the cell works. You've attached a pipette (A) to the largest cilia so that you can push and pull the hair cell bundle back and forth and observe the effects on the cell.

If you are in current clamp (recording the membrane voltage), draw the response you would get at pipette B by moving pipette A in a sinusoidal pattern (shown in black), first to the RIGHT and then to the LEFT. Label your axes (numbers not needed). (2 points)



You switch to voltage clamp (now recording the membrane voltage) and you push pipette A to the RIGHT and keep it there for 200 msec (shown below in black). Assuming the channel can pass a maximum of 200 pA of current, draw the response on the axes below including 100 msec before and 100 msec after you move the hair bundle. Label your axes. (3 points)



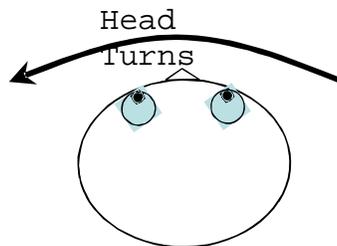
In a sentence or two, explain what mechanism could lead to this type of behavior. (1 point)

Relaxation of the tiplink, which gates the channel, down the side of the cilia would cause the channel to close.

13. Which of the following are true about the auditory system? (3 points)
- external pinnae are required for human detection of sound elevation
 - LSO gets excitatory input from both ears
 - Neurons sensitive to ILD (Interaural Level Disparity) provide information about location of a sound source but have broad frequency tunings.
 - Hair cells axons form glutamatergic synapses onto cochlear nucleus neurons.
 - Organization of hair cell polarity within the utricle and semicircular canals are identical.

A,C

14. Given the head movement pictured (4 points):



Please circle the appropriate answer:

- | | | | |
|---|-------------|----|--------------|
| Direction of fluid motion in left horizontal canal | LEFT | or | RIGHT |
| Direction of fluid motion in right horizontal canal | LEFT | or | RIGHT |
| Excitatory deflection of stereocilia in ampulla on | LEFT | or | RIGHT |
| Hyperpolarization of hair cells in ampulla on | LEFT | or | RIGHT |
| Excitatory innervation of abducens nucleus on | LEFT | or | RIGHT |
| Contraction of medial rectus on | LEFT | or | RIGHT |
| Inhibition of lateral rectus on | LEFT | or | RIGHT |
| Net effect is that eyes move | LEFT | or | RIGHT |

15a. Consider the vestibular ocular reflex (VOR). This reflex detects angular *acceleration* of the head and counter-rotates the eyes. The motor neurons which project to the extraocular muscles exhibit firing rates proportional to the *position* of the eyes. We discussed two stages of “integration” which occur in this transformation from acceleration to position. Where in the VOR circuit are these two stages? (2 points)

ANSWER: The first stage is in the semicircular canal. The mechanics are “over-damped” resulting in a cupula deflection proportional to velocity. The second stage is in the neural circuit involving the nucleus prepositus hypoglossi and the medial vestibular nuclei (for horizontal eye movements).

15b. The VOR is very fast ~10 ms. But the fastest visually driven eye movements, optokinetic nystagmus and smooth pursuit have latencies of ~80 ms and ~100 ms respectively. This is one reason why you can read a book fine when you shake your head back and forth, but not when you shake the book at the same rate. Briefly describe for 1) the VOR and 2) visually driven eye movements, what makes them slow/fast. (4 points)

ANSWER:

1) VOR: direct mechanical coupling of sensory stimulus (angular acceleration of the head) and ion channel opening (via semicircular canal fluid→cupula→hair cell) is very fast. high spiking rate of sensory neurons—changes can be detected quickly. Fibers projecting from semicircular canals are large and fast. And there are few synapses between the hair cells and the extraocular muscles.

2) visually driven: primary reason it is slow is because of the retinal latency (which is long because of the signal transduction cascades underlying light detection).

16. Which if the following are true? (2 points)

- a) The utricle and saccule detect angular acceleration of the head.
- b) The vestibular ocular reflex can be suppressed during orienting head movements.
- c) The neurons projecting from a single semicircular canal respond to only one direction of angular acceleration.

ANSWER: (a) FALSE, (b) TRUE, (c) TRUE

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17. Match the neuron type with the appropriate description(s) (5 points):

- | | | |
|------------------|-------------|--|
| a. Renshaw Cell | ___3,4___ | 1. Mediate GTO inhibition of agonist muscle |
| b. Group 1a | ___3,6___ | 2. Prevent excessive muscle tension |
| c. Alpha motor | ___7___ | 3. Are considered interneurons |
| d. Propriospinal | ___3,5___ | 4. Stabilize motor neuron firing rates |
| e. Group 1b | ___1,2,3___ | 5. Lateral-Medial position determines length of neuronal process |
| | | 6. Innervate muscle spindle |
| | | 7. Innervate slow motor units |

18. You are referred a patient whose primary care physician suspects he has upper motor neuron disease, but is unable to diagnose a specific etiology. Name three signs you expect to see on physical examination (3 points):

1. **Weakness**
2. **Exaggerated Reflexes**
3. **Spasticity**

Also: Babinski reflex.

NOT: atrophy, fiber type grouping.

19. There are two main proprioceptive systems in peripheral muscle. What are their names and what does each of them tell the CNS about the muscle? (2 points)

1.

2.

ANSWER:

1) Muscle spindle – in parallel with the muscle fibers and signal muscle stretch (kept it dynamic range by input from gamma motor neurons).

2) Golgi tendon organ – in series with the muscle fibers and signal muscle tension

20. Match the cerebellar structure with its target or origin(s) (2 points):

- | | | |
|--------------------|-------|---------------------------------|
| 1. Parallel fibers | __C__ | A. Second-order sensory neurons |
| 2. Purkinje cells | __B__ | B. Deep cerebellar nuclei |
| 3. Climbing fibers | __D__ | C. Granule cells |
| 4. Mossy fibers | __A__ | D. Inferior olive |

21. Indicate all the following that are true about the cerebellum (3 points):

- Across the different functional areas of the cerebellum, the cortical structure is remarkably similar.
- Phylogenetically speaking, the lateral cerebellar hemisphere is the oldest part of the cerebellum.
- The spinocerebellum consists of the vermis and intermediate (paravermal) zones, plus their deep output nuclei.
- The interposed nuclei effect distal motor control on the same side of the body.
- There is a somatotopic map in the cerebellar cortex with respect to motor output, but not sensory input.
- The leading theory on how the cerebellum operates is that complex spikes provide an "error signal" used to modify parallel fiber input through long term depression of the parallel fiber-Purkinje cell synapse.

Answer: A, C, D, F

22. The prevailing model for Parkinson's disease explains how the loss of dopaminergic neurons of the substantia nigra (pars compacta) causes a change in the relative amount of activity in the direct and indirect pathways through the striatum, favoring the indirect over the direct pathway. What observations, both clinical and scientific, are not well-explained by this model? (4 points)

Answer: (1) D1 and D2 receptors may colocalize on medium spiny neurons. Thus, it is difficult to explain how the reduction in dopamine from SNpc specifically changes activity in one loop relative to the other. (2) The emergence of the pill-rolling tremor is not well explained by this model. Students may also mention that rigidity is not well explained.

23. In one inherited form of ALS, in which gene is the mutation found? What is one hypothesis explaining the cascade of events leading to disease symptoms? (2 points)

The mutation is in the gene encoding the protein SOD-1 (superoxide dismutase). Loss of function in SOD-1 leads to decreases in ATP levels and axonal transport, as well as an increase in free radical production and protein aggregation.

24. A patient enters your office complaining of recent head trauma. Since the injury, he has been experiencing wild flinging movements of his left hand and arm, and, occasionally, of the left leg. Given what you know about the basal ganglia, where would you expect to find damage, and why would damage to that nucleus of the basal ganglia cause the observed symptoms? (3 points)

The patient is experiencing hemiballismus. This most likely results from damage to the RIGHT Subthalamic nucleus. (STN). STN usually excites the Gpi. With reduced Gpi excitation, the thalamus is LESS inhibited, leading to these ballistic movements.

25. What is the most common pharmacological treatment for Parkinson's disease? For each of the two components of the treatment, explain its purpose and site of actions. Why is the treatment administered in this form? (3 points)

Parkinson's is most commonly treated through a combination of L-DOPA and carbi-DOPA. Dopamine does not cross the BBB and has some circulatory effects, therefore it is administered as the DA precursor L-DOPA, which can cross the BBB and is metabolised there to DA. This treatment is used to make up for the loss of DAergic neurons of the SNc in Parkinson's. Carbi-DOPA prevents peripheral metabolism of L-DOPA, thereby preventing its consumption and potentiation of peripheral side effects.