

## 9.14 Homework 4

due before Lecture 18.

KEY

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Write brief answers to as many of the following questions as you can. They are based on a reading of chapters 13-17 of the book *Brain Structure and Its Origins*.

- 1) Contrast collateral sprouting of axons and regeneration of axons.

Regeneration: re-growth, partial or complete, of a transected axon from, or near, the place the axon was transected.

Collateral sprouting of an undamaged axon can occur in axonal arbors in response to degeneration of endings of nearby axons. It can also occur in axonal endings of axons which have suffered the loss of other terminal arbors. In either case, the sprouting may not be near the site of damage.

- 2) Describe membrane incorporation in growing axons.

Membrane is transported down the growing axons from the cell bodies in the form of small vesicles, which fuse to the axonal membrane at the growth cone. This also occurs at swellings along the axon.

- 3) Study the model of a growth cone depicted in figure 13.3. Describe the dynamics of axon growth using the concepts of fundamental cellular events named by Lewis Wolpert (chapter 8). [At least three of the concepts in bold font should be included in the answer.]

Filopodia extend from the growth cone, with tips that contain cell **adhesion** molecules in the membrane. The filopodia extend and contract back towards the growth cone. When the tips adhere to a substrate, the **contraction** pulls on the growth cone. The front edge of the growth cone is **moved** (pulled) in a direction determined by the vector sum of the forces created by all the filopodia that are adhering to the substrate. The axon **grows** as the back of the growth cone forms the axonal trunk and the size of the growth cone is maintained by incorporation of membrane of vesicles being transported in an anterograde direction from the cell body.

- 4) What is the major conclusion that can be drawn from Hibbard's experiment on transplanted amphibian Mauthner cells of the hindbrain? (I.e., what does his result mean?)

His result means that the substrate (the tissue of the hindbrain) contains a directional signal that determines the caudalward direction of growth of the axons of the Mauthner cells.

- 5) What is the protein "nogo" and what might it mean for attempts to promote axonal regeneration in the mature central nervous system?

Nogo is a membrane protein in oligodendrocytes. The protein inhibits the growth of axons that contact it. Since oligodendrocyte membranes form myelin, the myelinated axons of the mature CNS can be expected to inhibit the growth of axons, thus inhibiting regeneration.

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- 6) Describe an example of selective repulsion of axon growth into a structure like the optic tectum. What molecules are involved in the case of the developing retinotectal connections?

When axons from the temporal retina grow into the optic tectum from the rostral side, they grow readily through the rostral half of the tectum but appear to be repelled from the caudal half. Axons from the nasal retina are not repelled like this, since they grow into the caudal half of the tectum.

The molecules involved are ephrins in the tectum and ephrin receptors in the retinal neurons and their axons (Eph receptors). Gradients of different ephrins and Eph receptors are found across the tectum and across the retina.

- 7) Describe several of the factors that can influence the amount of collateral sprouting of axons. Separate intrinsic and extrinsic factors.

Extrinsic factors: Growth factors (like neurotrophin molecules), availability of vacant synaptic space, electrical activity of the axons.

Intrinsic factor: The growth vigor of the axon is affected not only by the above factors but also by the total amount of end arbor the axon has formed (or the number of synapses it has formed).

- 8) Describe **one method** that has been used to elicit axonal regeneration in the CNS of adult animals, with a return of function.

- Short segments of peripheral nerve have been cut from the leg of the animal with a brain lesion. These segments have been implanted so as to form bridges over the site of a transection of the optic tract. Axons that have been transected will grow into a peripheral nerve segment, supported by Schwann cells, grow across the bridge into the denervated tissue on the other side where they are able to form functional synapses.
- A very small amount of a self-assembling peptide discovered at MIT has been injected in water solution into the site of transection of the optic tract of hamsters. The peptide self-assembles into a gel that acts as a scaffold that supports axonal growth, and the optic-tract axons will regrow across the wound and form functional terminations on the more caudal side.

- 9) Contrast two types of initiation of movement by describing a specific example of locomotion initiated from the hypothalamus and a specific example of locomotion initiated because of visual input.

- Food deprivation causes increase in activity of hypothalamic cells which correspond to a strong hunger drive. This initiates locomotion necessary for foraging activity.

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[Student may also mention increased activity in the hypothalamic locomotor area and the midbrain locomotor area, but this is not essential for this part of an answer.]

- A small mammal sees an overhead raptor that may be approaching. This activates superior colliculus neurons that activate a descending ipsilateral pathway that causes escape locomotion. [The student may also mention that the pathway goes to the midbrain locomotor area.]

10) How is locomotion modulated by activity in structures of the hindbrain, regardless of how this locomotion was initiated? Name a descending pathway from the hindbrain whereby this modulation is accomplished.

Locomotion is modulated/ influenced by vestibular activity. Such activity activates axons of the vestibulospinal tract. [Student may also mention, or as an alternative describe, the fastigiospinal tract (cerebellospinal tract).]

11) Contrast the structure of the red nucleus of the midbrain in two species: a rat and a monkey.

The red nucleus is made up of a rostral parvocellular component and a caudal magnocellular component. In a monkey, the parvocellular component is much larger, and in a rat the magnocellular component is much larger.

12) Contrast the nature of peripheral synapses in the somatic motor system and the autonomic nervous system.

- In the somatic motor system, the axons of motor neurons make true synapses with striated muscle fibers—each synapse affecting only one muscle fiber.
- In the autonomic nervous system, an axon from an autonomic ganglion release its neurotransmitter less specifically when activated by action potentials, so that it affects multiple smooth muscle fibers or multiple gland cells. This is called apocrine activation rather than true synaptic activation.

13) Many of the dexterous movements that depend on the corticospinal tract are learned movements. How are innate movement patterns (fixed action patterns) different?

First of all, innate movement patterns are largely unlearned. Secondly, dexterous movements of an innate movement pattern may also use the corticospinal tract.

14) How might many learned movements depend on spinal “modules” more than on direct connections from cortex to motor neurons?

Many movements activate spinal modules that cause a hand or foot to move to a particular position in space. This simplifies learning to move the hand or foot to

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particular places since the descending pathway simply has to activate a specific combination of spinal modules. Activating each spinal neuron involved would require much more descending information, making the learning task more complex.

- 15) Destruction of medial hindbrain pathways in monkeys can cause drastic effects on movement abilities. Why is it that when such lesions are inflicted unilaterally, there is usually little effect?

The remaining unilateral pathway has terminations in the spinal cord that reach the contralateral as well as the ipsilateral side. Thus, there is redundancy in the pathways controlling the axial muscles, so an animal can quickly compensate for the loss of only the right or only the left descending pathway.

- 16) How can neuroanatomical experiments determine whether primary somatosensory cortex overlaps fully or partially with primary motor cortex?

The thalamic nucleus VL projects to the motor cortex, and the nucleus VP projects to the primary somatosensory cortex. The anatomist can use either retrograde or anterograde tracing to find out how much, if any, of the projections from these two nuclei overlap in the cortex.

- 17) How do we know that the generation of rhythmic neural activity, by whatever means, can be used to generate any conceivable temporal pattern of activity?

We know this from the mathematics of Fourier analysis, in which a waveform of any complexity can be represented as a summation of different sine waves, of different frequencies, phases, and amplitudes.

- 18) What are two different types of mechanisms whereby the overall state of all or much of the brain can be changed?

- 1) Chemical secretions into the cerebrospinal fluid.
- 2) Activation of a system of very widespread projections.

- 19) How have changes in brain state been measured by the recording of electrical potentials? (This is not much discussed in the textbook.) Discuss the adequacy or inadequacy of such a measure.

- Electroencephalograph recordings (EEG) show different rhythms and amplitudes when an human or animal is relaxed and quiet, wide awake and attending to novel inputs, drowsy, falling asleep, in deep sleep or in dream sleep.
- Such recordings have not indicated the very large number of different brain states that the known widespread axonal projections are capable of generating.

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