Case 6

Multiple Sclerosis: Myelin and Conduction Velocity

Meg Newton is a 32-year-old assistant at a horse-breeding farm in Virginia. She feeds, grooms, and exercises the horses. At age 27, she had her first episode of blurred vision. She was having trouble reading the newspaper and the fine print on labels. She had made an appointment with an optometrist, but when her vision cleared on its own, she was relieved and canceled the appointment. Ten months later, the blurred vision returned, this time with other symptoms that could not be ignored. She had double vision and a “pins and needles” feeling and severe weakness in her legs. She was even too weak to walk the horses to pasture.

Meg was referred to a neurologist, who ordered a series of tests. Magnetic resonance imaging (MRI) of the brain showed lesions typical of multiple sclerosis. Visual evoked potentials had a prolonged latency that was consistent with decreased nerve conduction velocity. Since the diagnosis, Meg has had two relapses, and she is currently being treated with interferon beta.

QUESTIONS

1. How is the action potential propagated in nerves (such as sensory nerves of the visual system)?

2. What is a length constant, and what factors increase it?

3. Why is it said that action potentials propagate “nondecrementally?”

4. What is the effect of nerve diameter on conduction velocity, and why?

5. What is the effect of myelination on conduction velocity, and why?

6. In myelinated nerves, why must there be periodic breaks in the myelin sheath (nodes of Ranvier)?

7. Meg was diagnosed with multiple sclerosis, a disease of the central nervous system, in which axons lose their myelin sheath. How does the loss of the myelin sheath alter nerve conduction velocity?
ANSWERS AND EXPLANATIONS

1. Propagation of action potentials occurs along nerve fibers by spread of local currents. At rest, the nerve fiber is polarized (i.e., inside negative with respect to outside). When an action potential occurs, the inward current of the upstroke of the action potential depolarizes the membrane and reverses the polarity at that site (i.e., that site briefly becomes inside positive). The depolarization then spreads to adjacent sites along the nerve fiber by local current flow, or electrotonic conduction, as shown in Figure 1-9. As the depolarization spreads electrotonically to adjacent areas, it decays. Thus, local currents are conducted decrementally, and as a consequence, the further from the site of the action potential, the smaller the local depolarization. Importantly, though, if these local currents depolarize an adjacent region to threshold, it will fire an action potential (i.e., the action potential is propagated).

![Figure 1-9 Unmyelinated axon showing spread of depolarization by local current flow. Box shows active zone where action potential has reversed the polarity.](image)

2. Length constant is defined as the distance from the original site of depolarization (the site of the action potential) where the potential has fallen, or decayed, to 63% of its original value; the longer the length constant, the less the decay, and the further local current spread occurs along the axon. Length constant can be increased in two ways: increasing membrane resistance (such that current is forced to flow down the axon interior rather than leaking out across the membrane) and decreasing internal resistance of the axon (such that current flows more readily along the axon interior).

3. As described before, local currents are conducted along axons decrementally. Why, then, is it said that action potentials propagate nondecrementally? In the process of local current spread, if a neighboring site is depolarized to threshold, it fires an action potential. This regenerative process, by creating a new action potential at a site further along the axon, restores the full extent of depolarization. Depolarization now spreads from this new site and depolarizes neighboring sites to threshold; those neighboring sites fire action potentials, continuing the process along the axon. The restorative function that periodically creates new action potentials ensures that the depolarization does not die out along the length of the axon.

4. Increased diameter is associated with decreased internal resistance of the nerve fiber, which increases the length constant. Increased length constant leads to increased conduction velocity, because the local currents will spread further down the axon.

5. Myelination increases conduction velocity. Myelin is an insulator of axons, increasing membrane resistance and decreasing membrane capacitance. By increasing membrane resistance, current is forced to flow down the axon interior and less current is lost across the cell membrane (increased length constant); because more current flows down the axon, conduction velocity is increased. By decreasing membrane capacitance, local currents depolarize the membrane more rapidly, which also increases conduction velocity.

6. In order for action potentials to be conducted in myelinated nerves, there must be periodic breaks in the myelin sheath (at the nodes of Ranvier). The nerve action potential consists of depolarization (due to opening of cell membrane Na+ channels), followed by repolarization (due
to opening of cell membrane K⁺ channels). Opening of these channels permits the flow of ions across the membrane that produces the characteristic depolarization and repolarization of the action potential. In myelinated nerves, these Na⁺ and K⁺ channels are not distributed along the entire axon membrane, but are concentrated at nodes of Ranvier. Thus, at the nodes, the ionic currents, necessary for the action potential, can flow across the membrane. Between nodes, membrane resistance is very high and current is forced to flow rapidly down the nerve axon to the next node, where the next action potential can be generated. Thus, the action potential appears to “jump” from one node of Ranvier to the next, which is called saltatory conduction (Figure 1-10). If there were no breaks in the myelin sheath, there would be no regions of ion channel density (e.g., Na⁺ channels) where action potentials could occur to restore the full level of depolarization.

![Myelinated axon. Action potentials can occur at nodes of Ranvier.](image)

7. Multiple sclerosis is the most common demyelinating disease of the central nervous system. Loss of the myelin sheath around nerves causes a decrease in membrane resistance, which means that current “leaks out” across the membrane during electrotonic conduction. In other words, current decays more rapidly (decreased length constant) as it flows down the axon and, because of this decay, may be insufficient to generate an action potential when it reaches the next node of Ranvier.

**Key topics**

- Capacitance (or membrane capacitance)
- Conduction velocity (of action potential)
- Electrotonic conduction
- Length constant
- Local currents
- Multiple sclerosis
- Myelin
- Nodes of Ranvier
- Propagation of action potential
- Resistance (or membrane resistance)
- Saltatory conduction