Lecture Outline for Integrated Basic Health Sciences for Pharmacy

Physiology Component of Module : Cell Biology

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Membrane Potential (Ch3)

- Resting membrane potential – Voltage or potential difference across a plasma membrane
- Ranges from –50 to –100 mV
  - Results from Na^+ and K^+ concentration gradients across the membrane (see Figure 3.15)
  - Differential permeability of the plasma membrane to Na^+ and K^+
- Steady state – potential maintained by active transport of ions

Membrane Potential (Ch 11)

Electricity Definitions

- Voltage (V) – measure of potential energy generated by separated charge
- Potential difference – voltage measured between two points
- Current (I) – the flow of electrical charge between two points
- Resistance (R) – hindrance to charge flow
- Insulator – substance with high electrical resistance
- Conductor – substance with low electrical resistance

Electrical Current and the Body

- Reflects the flow of ions rather than electrons
- There is a potential on either side of membranes when:
  - The number of ions is different across the membrane
  - The membrane provides a resistance to ion flow

Role of Ion Channels

- Types of plasma membrane ion channels:
  - Passive, or leakage, channels – always open
  - Chemically gated channels – open with binding of a specific neurotransmitter
  - Voltage-gated channels – open and close in response to membrane potential

  - Mechanically gated channels – open and close in response to physical deformation of receptors

Operation of a Gated Channel (see Figure 11.6a)

- Example: Na^+-K^+ gated channel
- Closed when a neurotransmitter is not bound to the extracellular receptor
  - Na^+ cannot enter the cell and K^+ cannot exit the cell
- Open when a neurotransmitter is attached to the receptor
  - Na^+ enters the cell and K^+ exits the cell

Operation of a Voltage-Gated Channel (see Figure 11.6b)

- Example: Na^+ channel
- Closed when the intracellular environment is negative
  - Na^+ cannot enter the cell
- Open when the intracellular environment is positive
  - Na^+ can enter the cell

Gated Channels

- When gated channels are open:
  - Ions move quickly across the membrane
  - Movement is along their electrochemical gradients
  - An electrical current is created
  - Voltage changes across the membrane

Electrochemical Gradient

- Ions flow along their chemical gradient when they move from an area of high concentration to an area of low concentration
- Ions flow along their electrical gradient when they move toward an area of opposite charge
- Electrochemical gradient – the electrical and chemical gradients taken together

Resting Membrane Potential (V_r)

- The potential difference (–70 mV) across the membrane of a resting neuron
- It is generated by :
  - different concentrations of Na^+ and K^+ across the membrane
  - differential permeability of the neurilemma to Na^+ and K^+
- It is maintained by :
  - Operation of the sodium-potassium pump

Measuring Membrane Potential (see Figure 11.7)

Resting Membrane Potential (V_r) (see Figure 11.8)

Membrane Potentials: Signals
- Used to integrate, send, and receive information
- Membrane potential changes are produced by:
  - Changes in membrane permeability to ions
  - Alterations of ion concentrations across the membrane
- Types of signals – graded potentials and action potentials

Changes in Membrane Potential (see Figure 11.9)
- Changes are caused by three events
  - Depolarization – the inside of the membrane becomes less negative
  - Repolarization – the membrane returns to its resting membrane potential
  - Hyperpolarization – the inside of the membrane becomes more negative than the resting potential

Changes in Membrane Potential
Graded Potentials
- Short-lived, local changes in membrane potential
- Decrease in intensity with distance
- Magnitude varies directly with the strength of the stimulus
- Sufficiently strong graded potentials can initiate action potentials

Graded Potentials (see Figure 11.10)
Graded Potentials
- Voltage changes are decremental
- Current is quickly dissipated due to the leaky plasma membrane
- Only travel over short distances

Action Potentials (APs) (see Figure 11.11)
- A brief reversal of membrane potential with a total amplitude of 100 mV
- Action potentials are only generated by muscle cells and neurons
- They do not decrease in strength over distance
- They are the principal means of neural communication
- An action potential in the axon of a neuron is a nerve impulse

Action Potential: Resting State ①
- Na^+ and K^+ channels are closed
- Leakage accounts for small movements of Na^+ and K^+
- Each Na^+ channel has two voltage-regulated gates
  - Activation gates – closed in the resting state
  - Inactivation gates – open in the resting state

Action Potential: Depolarization Phase ②

- Na^+ permeability increases; membrane potential reverses
- Na^+ gates are opened; K^+ gates are closed
- Threshold – a critical level of depolarization (-55 to -50 mV)
- At threshold, depolarization becomes self-generating

Action Potential: Repolarization Phase ③

- Sodium inactivation gates close
- Membrane permeability to Na^+ declines to resting levels
- As sodium gates close, voltage-sensitive K^+ gates open
- K^+ exits the cell and internal negativity of the resting neuron is restored

Action Potential: Hyperpolarization ④

- Potassium gates remain open, causing an excessive efflux of K^+
- This efflux causes hyperpolarization of the membrane (undershoot)
- The neuron is insensitive to stimulus and depolarization during this time

Action Potential: Role of the Sodium-Potassium Pump

- Repolarization
  - Restores the resting electrical conditions of the neuron
  - Does not restore the resting ionic conditions
- Ionic redistribution back to resting conditions is restored by the sodium-potassium pump

Phases of the Action Potential

- 1 – resting state
- 2 – depolarization phase
- 3 – repolarization phase
- 4 – hyperpolarization

Propagation of an Action Potential (Time = 0ms) (see Figure 11.12a)

- Na^+ influx causes a patch of the axonal membrane to depolarize
- Positive ions in the axoplasm move toward the polarized (negative) portion of the membrane
- Sodium gates are shown as closing, open, or closed

Propagation of an Action Potential (Time = 2ms) (see Figure 11.12b)

- Ions of the extracellular fluid move toward the area of greatest negative charge

- A current is created that depolarizes the adjacent membrane in a forward direction
- The impulse propagates away from its point of origin

Propagation of an Action Potential
(Time = 4ms) (see Figure 11.12c)

- The action potential moves away from the stimulus
- Where sodium gates are closing, potassium gates are open and create a current flow

Threshold and Action Potentials

- Threshold – membrane is depolarized by 15 to 20 mV
- Established by the total amount of current flowing through the membrane
- Weak (subthreshold) stimuli are not relayed into action potentials
- Strong (threshold) stimuli are relayed into action potentials
- All-or-none phenomenon – action potentials either happen completely, or not at all

Coding for Stimulus Intensity (see Figure 11.13)

- All action potentials are alike and are independent of stimulus intensity
- Strong stimuli can generate an action potential more often than weaker stimuli
- The CNS determines stimulus intensity by the frequency of impulse transmission

Absolute Refractory Period (see Figure 11.14)

- Time from the opening of the Na^+ activation gates until the closing of inactivation gates
- The absolute refractory period:
  - Prevents the neuron from generating an action potential
  - Ensures that each action potential is separate
  - Enforces one-way transmission of nerve impulses

Relative Refractory Period (see Figure 11.14)

- The interval following the absolute refractory period when:
  - Sodium gates are closed
  - Potassium gates are open
  - Repolarization is occurring
- The threshold level is elevated, allowing strong stimuli to increase the frequency of action potential events

Conduction Velocities of Axons (see Figure 11.15)

- Conduction velocities vary widely among neurons

- Rate of impulse propagation is determined by:
  - Axon diameter – the larger the diameter, the faster the impulse
  - Presence of a myelin sheath – myelination dramatically increases impulse speed

Saltatory Conduction

- Current passes through a myelinated axon only at the nodes of Ranvier
- Voltage-gated Na^+ channels are concentrated at these nodes
- Action potentials are triggered only at the nodes and jump from one node to the next
- Much faster than conduction along unmyelinated axons (continuous conduction)

Multiple Sclerosis (MS)

- An autoimmune disease that mainly affects young adults
- Symptoms: visual disturbances, weakness, loss of muscular control, and urinary incontinence
- Nerve fibers are severed and myelin sheaths in the CNS become nonfunctional scleroses
- Shunting and short-circuiting of nerve impulses occurs

Multiple Sclerosis: Treatment

- The advent of disease-modifying drugs including interferon beta-1a and -1b, Avonex, Betaseran, and Copazone:
  - Hold symptoms at bay
  - Reduce complications
  - Reduce disability

END OF OUTLINE