Life 26 - Chemical communication - Raven & Johnson Ch 56

Objectives

1: Compare the action of a typical hormone with that of a neuron.

2: Know the characteristics of the four chemical classes of hormones.

3: Understand the two primary mechanisms of hormone action, depending on whether the hormone enters the cell or not.

4: Describe the actions of the cAMP and IP_3/Ca^{2+} second messenger systems.

5: Understand the role of norepinephrine (noradrenaline) as a transmitter in the sympathetic nervous system and as a neurohormone.

Chemical communication

Some regulation is achieved at the biochemical level – seen feedback inhibition of glycolysis and aerobic respiration in the production of ATP

Other regulation uses one or both of the two regulatory systems in animals, the nervous and endocrine systems

Last two lectures describe the endocrine system, especially comparison with, and links to, the nervous system

Seen chemical communication between individual cells in **Neurobiology** - neurotransmitters at chemical synapses

Chemicals also used for long-range communication between groups of cells in different parts of the body - hormones of the endocrine system

Neurotransmitters diffuse short distances only, in the synaptic cleft, usually affect only one post-synaptic target cell (Fig. 56.2)

Hormones are secreted by endocrine (ductless) glands, pass in the blood circulation and reach many cells, but affect only some of them. These target cells have specific receptors, which other cells lack

Other categories of chemical communication:
1: Paracrine regulation, where intercellular messengers act within one organ, not carried in blood. E.g. immune system, growth factors
2: Pheromones, where chemicals released into the environment, for communication between animals. E.g. reproduction

Endocrine system includes both specialised organs (thyroid, pituitary, adrenal etc) and organs with other functions as well (brain, reproductive organs)

The only limitation to the chemical nature of a hormone is that its structure must be complex enough to permit a specific receptor. A variety of chemicals act as hormones

1: Peptides. Have less than 100 (usually 3-14) amino acids. E.g. growth hormone releasing hormone (10 amino acids), insulin

2: Glycoproteins. More than 100 amino acids, and carbohydrate groups. E.g. growth hormone (191 amino acids), follicle-stimulating hormone

3: Amines. Modified amino acids, derived from tyrosine or tryptophan. E.g. thyroxine, also adrenaline (epinephrine) from the adrenal medulla (inner part of adrenal gland)

4: Steroids. Lipids derived from cholesterol, one 5-carbon and three 6-C rings (Fig. 56.4). E.g. testosterone, estradiol (sex steroids), also cortisol & other corticosteroids from adrenal cortex (outer part of adrenal gland)

Steroids and thyroxine are lipophilic (fat soluble), all other hormones are polar or hydrophilic (water soluble) – an important distinction for their action

Lipophilic hormones

These enter cells easily, through the lipid cell membrane. Steroids are lipids themselves, thyroxine derived from the nonpolar amino acid tyrosine. All have similar mechanism of action (Fig. 56.5)

Not soluble in water/plasma, carried in the blood attached to protein carrier molecules. Hormone dissociates from carrier and passes through cell membrane (step 1)

Then binds to specific receptor protein (step 2) in the cytoplasm or nucleus of a target cell

Hormone-receptor complex enters (or already in) the nucleus, binds to specific region of the DNA (step 3)

Binding at the hormone response element of the DNA stimulates transcription at the site, produces messenger RNA coding for a specific protein (step 4)

This protein is synthesised in the cytoplasm (step 5) - usually an enzyme which affects the metabolism of the target cell

Action of thyroxine is similar (Fig. 56.6). Thyroid gland produces thyroxine or T_4 (4 iodines - tetraiodothyronine), & smaller amounts of T_3 (3 iodines - triiodothyronine)

Both T_4 and T_3 enter cells through cell membrane. T_4 is converted to T_3, which enters the nucleus and binds to nuclear receptor proteins. The hormone-receptor complex binds to DNA & stimulates transcription

Hydrophilic hormones

All other hormones are too large or too polar to cross the cell membrane. They bind to receptor proteins on the outer surface of the cell membrane. E.g. adrenaline (epinephrine) (Fig. 56.7)

Hormone does not enter the cell, so needs a second messenger within the target cell (hormone is the first messenger, from the endocrine gland)

The interaction between the hormone and the receptor protein is brief and reversible, causes the cell membrane to release the second messenger

The hormone may then travel to a second target cell. Eventually enzymes (often in the liver) degrade the hormone to an inactive form

There are many second messenger systems. Adrenaline binds with two types of receptors, α-adrenergic and β-adrenergic receptors, each with a different second messenger

Cyclic AMP second messenger system
β receptors (step 1) have cyclic adenosine monophosphate (cAMP) as the second messenger (Fig. 56.7)

Receptor protein is associated with other membrane proteins called G proteins, for guanosine triphosphate (GTP)-binding protein

G protein is bound to receptor protein on inner side of cell membrane. When adrenaline binds to outer side of the receptor protein, G protein is released from inner side. In activated form due to GTP

Activated G protein diffuses to another membrane-bound protein, adenylyl cyclase, an enzyme that catalyses the formation of cAMP from ATP (step 2)

cAMP then binds to and activates protein kinase-A (step 3). This enzyme adds phosphate groups to specific proteins to activate them

Phosphate groups are added to different proteins in different target cells, therefore adrenaline has different effects on different tissues

In liver cells protein kinase-A activates phosphorylase, which converts glycogen to glucose (step 4)

Adrenaline thus causes glucose secretion into the blood, to provide energy for cells, as part of the “fight or flight” reaction

Other proteins are activated in cardiac muscle cells, cause the heart to beat faster and more forcefully as part of the same reaction

IP_3 / Ca^{2+} second messenger system
Adrenaline stimulates other cells with α-adrenergic receptors (step 1) through a different second messenger system (Fig. 56.8)

There is a different G protein, which activates another membrane-bound enzyme phospholipase

Phospholipase cleaves some membrane phospholipids to give the second messenger inositol triphosphate (IP_3) (step 2)

IP_3 binds to receptors on the endoplasmic reticulum (step 3). This organelle accumulates Ca^{2+} ions by removing them from the cytoplasm

Binding IP_3 stimulates the endoplasmic reticulum to release the stored Ca^{2+} (step 4)

Ca^{2+} then binds to the cytoplasmic protein calmodulin (step 5). The Ca^{2+} - calmodulin complex functions like cAMP

The complex activates other proteins, e.g. another protein kinase that adds phosphate to different proteins to activate these in turn

Why different second messengers? - The advantage of having multiple systems is that target cells can respond to different hormones in different ways, each via a different second messenger

E.g. adrenaline and insulin have opposite effects on liver cells

Adrenaline leads to hydrolysis of glycogen to glucose, via cAMP. Insulin leads to synthesis of glycogen from glucose, via another second messenger

Other polar hormones do not use second messengers, but alter the shape of an ion channel in the cell membrane, to open or close it

E.g. some hormones affecting muscle cells, open or close Ca^{2+} channels in the membrane, increase or decrease muscle contraction

Neuroendocrine secretion

Some of the cells that produce hormones are neurons. These are known as neurohormones, and the cells are neuroendocrine cells

Some neurohormones are also neurotransmitters, in the nervous system. E.g. noradrenaline (norepinephrine), a form of adrenaline, is a transmitter in the sympathetic nervous system

Usually think of the voluntary nervous system which includes sensory neurons, interneurons, and motor neurons

These obtain information from the environment, process it, and control skeletal muscles to give conscious behaviour, as well as reflexes

Motor neuron cell bodies are in the central nervous system (CNS - brain plus spinal cord), in the spinal cord

Motor neuron axons pass out of the CNS, and synapse with skeletal muscle cells as their effector organs. (Schmidt-Nielsen Fig. 12.4)

The peripheral (nerve-muscle) transmitter is acetylcholine. Also several other central neurotransmitters, between neurons in the CNS

There is another system which controls involuntary activity, mostly of smooth muscle, e.g. in the gut, blood vessels, also rate of heart beat

This is the autonomic nervous system, which has two divisions, the sympathetic and the parasympathetic

The two divisions innervate the same organs, but have antagonistic effects - one excites where the other inhibits

The autonomic nervous system is controlled by the brain, through axons passing down the spinal cord

Sympathetic neuron cell bodies are in ganglia near the spinal cord, while parasympathetic neuron cell bodies are in ganglia near the effector organs

The neurotransmitter in the parasympathetic system is acetylcholine, also between the central nervous system and the sympathetic neuron

The neurotransmitter between sympathetic axon and effector organ is noradrenaline (Schmidt-Nielsen Fig. 12.4)

Acetylcholine and noradrenaline thus usually have opposite effects on effector organs – they are used by the two antagonistic divisions of the autonomic nervous system

E.g. the control of the heart rate. Noradrenaline increases the heart rate, while acetylcholine slows the heart

Acetylcholine is thus inhibitory here, rather than excitatory as in skeletal muscle

This is an important point about neurotransmitters and hormones. The effect depends on the response of the target cells, not on the characteristics of the chemical messenger

Noradrenaline is a hormone as well as a neurotransmitter, released into the blood circulation by the adrenal medulla

Adrenal medulla is a neuroendocrine tissue, derived from neural ectoderm in development, the same cell layer as the nervous system

Noradrenaline in the blood has similar effects to stimulation of the sympathetic nervous system. It acts on same target cells, both as neurotransmitter and hormone

Neuroendocrine cells have similar structure to other neurons, and produce a resting potential, but are specialised for synthesis, storage and secretion of hormones

They produce action potentials, related to the control of secretion. The amount of secretion is proportional to the frequency of action potentials

Neurohormones are produced in the cell body. Some neuroendocrine cells have long axons, and the hormones pass down the axon to reach blood capillaries. Site of release is called a neurohaemal organ