Sem – IV (PG)

Paper ZOO-402

Group B : Neuro-Immuno Endocrinology

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Neuro-immuno endocrine pathways (1)

THE BODY'S THREE COMMUNICATION SYSTEMS:

The body has three different communication systems: the nervous system, the endocrine system and the immune system, each of which uses its own type of chemical messenger. Nerve cells communicate through the release of neurotransmitters, endocrine glands by hormones and the immune system by cytokines. These three systems are not independent; each one interacts with the other two, as outlined in Figure 1. Because these systems interact, they are often referred to as the neuro-endocrine, neuro-immune or neuro-immunoendocrine systems. To designate the influence of these systems on behaviour, the terms psycho-neuroendocrinology and psycho-neuroimmunology have been coined. The nervous system controls the release of hormones and can influence the release of the cytokines from the immune system. Hormones and other chemical messengers modulate the activity of both the nervous system and the immune system. Likewise, the lymphoid system can modulate neural activity and the release of hormones by the release of cytokines. While cognitive-sensory stimuli influence neural, immune and endocrine activity through the brain and nervous system, non-cognitive stimuli, such as bacteria and viruses influence these systems through their action on the immune system. These three systems may be integrated through the actions of common receptor mechanisms.

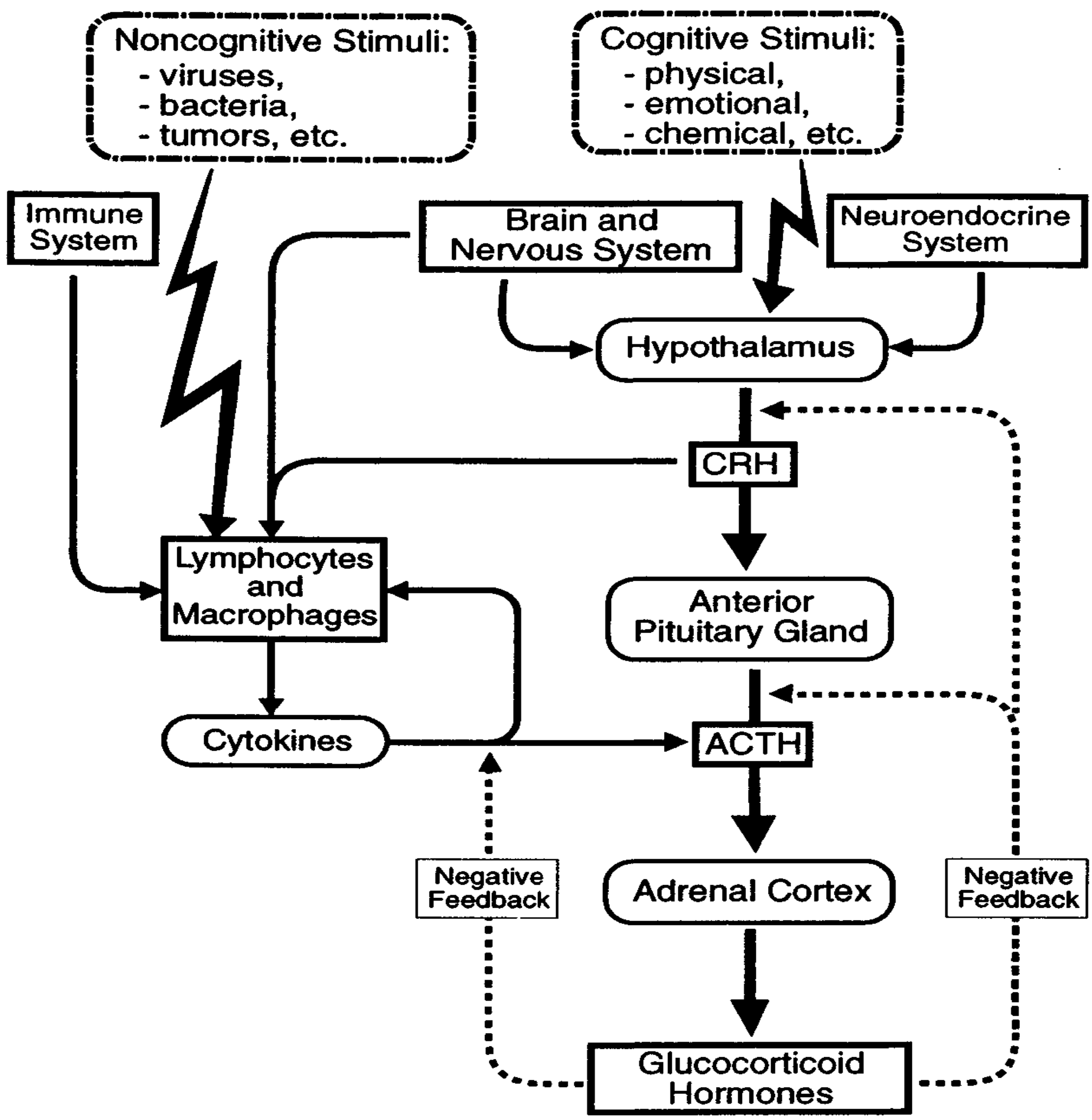

Fig 1: The body's three communication systems do not act independently. The brain and nervous system influence the neuroendocrine and immune systems, which also influence each other and the brain. This example shows that cognitive stimuli activate the neuroendocrine system through the brain and nervous system and the resulting neural and endocrine activation influences the release of cytokines from cells of the immune system. Non-cognitive stimuli such as viruses and bacteria first activate the immune system and the resulting release of cytokines activates the neuroendocrine system. Using the example of the hypothalamic-pituitary-adrenal system, the hypothalamic hormone CRH influences cytokine release from the cells of the immune system, which in turn influences ACTH release. Glucocorticoids have negative feedback on the cytokines as well as the hypothalamic and pituitary hormones.

METHODS OF COMMUNICATION BETWEEN CELLS

As shown in Figure 2, chemical messengers may communicate with their target cells through endocrine, paracrine, autocrine, neuroendocrine or neurocrine mechanisms.

- ENDOCRINE COMMUNICATION -

Endocrine cells release their hormones into the bloodstream and these hormones travel through the circulation to distant target cells. For example, thyroid stimulating hormone (TSH) is released from the pituitary gland and travels through the bloodstream to stimulate its target cells in the thyroid gland.

- PARACRINE COMMUNICATION -

Endocrine cells also release hormones which act on adjacent cells. These hormones may diffuse from one cell to the next, or go into the bloodstream, but travel only a very short distance. Paracrine secretion is, therefore, a localized hormone action. This happens, for example, in the testes. In order to produce sperm, the Sertoli cells must be stimulated by testosterone from the adjacent interstitial cells. Paracrine secretion is also important in the immune system.

- AUTOCRINE COMMUNICATION -

If a cell releases a hormone or neurotransmitter which has a direct feedback effect on the secretory cell, this is referred to as autocrine action. A specific example of autocrine communication would be a neurotransmitter acting presynaptically to modify its own release.

- NEUROENDOCRINE COMMUNICATION -

Neuroendocrine (neurosecretory) cells are modified neurons which release neurohormones either into the peripheral circulatory system, so that they can stimulate distant target cells (e.g. the release of oxytocin by the posterior pituitary to stimulate targets cells in the uterus), or into the hypophyseal portal vessels to induce the release of pituitary hormones (e.g. luteinizing hormone releasing hormone released from the hypothalamus to stimulate the release of luteinizing hormone from the anterior pituitary).

- NEUROCRINE COMMUNICATION -

Neurons (nerve cells) release discrete chemical messengers which are active over very short distances. Neurons which release neurotransmitters into a synapse to stimulate or inhibit a postsynaptic cell are one example of neurocrine secretion (e.g. the release of acetylcholine). A second example is the case of a neuropeptide, acting as a neuromodulator, released from a neural cell, which stimulates a receptor on a nearby cell and thus regulates its activity (e.g. somatostatin or substance P).

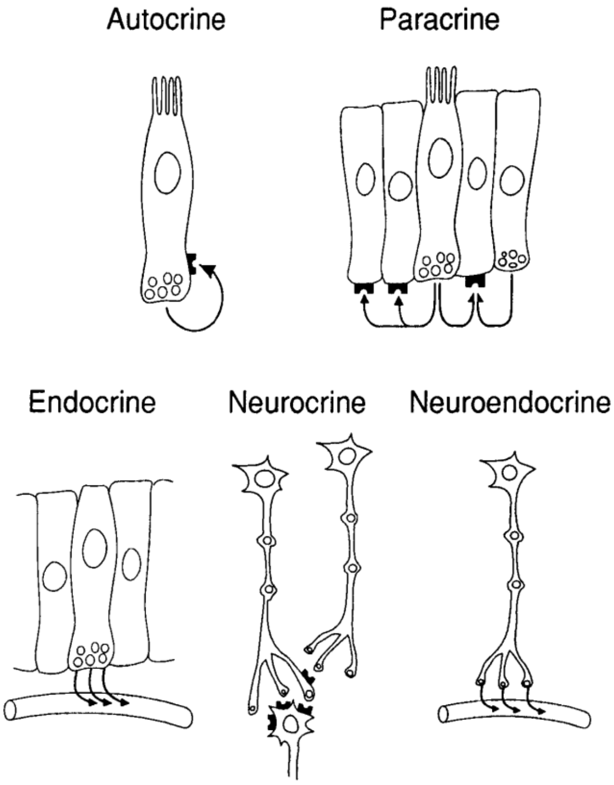

Fig 2: Methods of communication between cells of the neuroendocrine system. In autocrine communication, hormones act on the cells that release them. In paracrine communication, hormones act on adjacent cells as occurs in the testes, gastrointestinal tract and pituitary gland. Endocrine communication occurs when hormones are released into the bloodstream and act on cells at distant sites throughout the body. Neurocrine communication occurs when neurotransmitters are released from presynaptic cells into the synapse and act on receptors of postsynaptic cells in the central and peripheral nervous systems. Neuroendocrine secretion involves the release of neurohormones from neurosecretory cells in the hypothalamus, adrenal medulla and pineal gland.

TYPES OF CHEMICAL MESSENGERS RELATED TO NEURO-IMMUNO ENDOCRINOLOGY

- 'True' Hormones

These are (a) chemical messengers which are (b) synthesized in ductless (endocrine) glands and (c) secreted into the blood stream. They (d) act on specific target cell receptors and (e) exert specific physiological regulatory actions in the target cells.

- Neurohonnones

Hormones which are released by neurosecretory cells (modified nerve cells) via the posterior pituitary into the circulation (e.g. oxytocin and vasopressin) or via the portal system, into the anterior pituitary.

- Neurotransmitters

These are released by presynaptic nerve cells into a synapse (e.g. acetylcholine, dopamine, adrenaline, etc.) where they stimulate receptors on postsynaptic nerve cells.

- Pheromones

These are (a) volatile chemical messengers which are (b) synthesized in exocrine (duct) glands and (c) secreted into the environment. They (d) act on other individuals, usually of the same species, through olfactory or gustatory receptors and (e) alter behavior (releaser effects) or the neuroendocrine system (primer effects).

- Cytokines

Hormone-like factors released from lymphocytes, macrophages and other cells of the immune system which regulate the activity of cells of the immune and neuroendocrine systems (e.g. interferon γ and the interleukins).

NEUROREGULATORS: NEUROMODULATORS AND NEUROPEPTIDES

Some hormones synthesized in endocrine glands are also produced in the brain and act as neurotransmitters (e.g. cholecystokinin); many chemical messengers have receptors in the brain and thus influence brain function. These chemicals may be called neuroregulators, neuropeptides, or neuromodulators.

- NEUROREGULATORS

A 'neuroregulator' is a general term for any chemical messenger which regulates the activity of a nerve cell. A neuroregulator can be either a neurotransmitter or a neuromodulator.

- NEUROTRANSMITTERS

A neurotransmitter is a chemical messenger released by a presynaptic nerve cell that acts via the synapse to stimulate receptors on a postsynaptic nerve cell.

- NEUROMODULATORS

A neuromodulator is a chemical released by a neural, endocrine, or other type of cell and acts on a neuron to modulate its response to a neurotransmitter. One mechanism through which neuromodulators influence neural activity is by altering the permeability of the nerve cell membrane to ions such as sodium or chloride. Steroid hormones such as estrogen or testosterone act as neuromodulators, as do peptide hormones such as cholecystokinin.

Neuroregulator A neurotransmitter or other chemical (neuromodulator) which alters nerve cell activity

Neurotransmitter	Neuromodulator
A chemical messenger	A chemical messenger
Alters neural activity	Alters neural activity
Released from a presynaptic cell	Released from neural and non-neural cells (supporting cells, neuroendocrine cells, endocrine glands).
Acts via the synapse on the receptors of the postsynaptic cell	Acts non-synaptically on both the presynaptic and postsynaptic cell to alter synthesis, storage, release and reuptake of the neurotransmitter
Can be a monamine, indoleamine, or catecholamine	Can be a steroid or neuropeptide hormone or non-hormonal peptide

Neuropeptide A hormonal or non-hormonal peptide which acts as a neuromodulator

- NEUROPEPTIDES

Neuropeptides are hormone or non-hormone peptides that act as neuromodulators. Thus, ACTH and insulin are both peptide hormones in the body and neuropeptides in the brain. LH-RH is a peptide hormone and also a neuropeptide which acts as a neuromodulator, and is thus a neuroregulator. Bombesin and neurotensin are non-hormonal peptides which modulate neural activity.

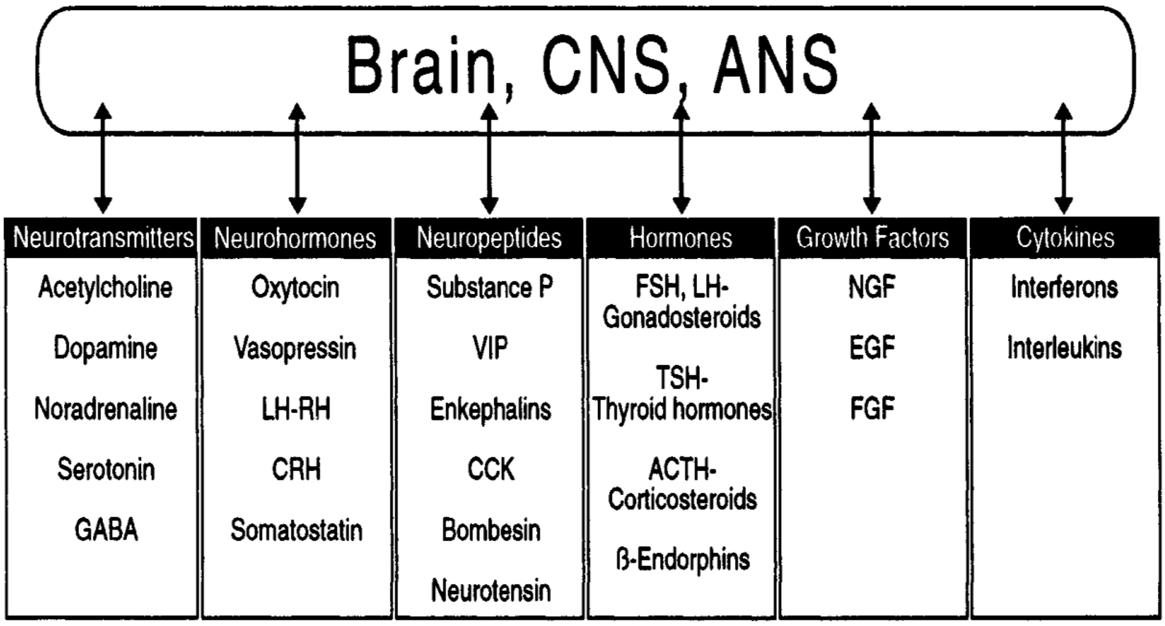

Fig 3: Some of the mechanisms through which the brain interacts with and regulates the secretion of the chemical messengers of the neuroendocrine and neuroimmune systems. The brain, central nervous system (CNS) and autonomic nervous system (ANS) stimulate the release of neurotransmitters, neurohormones and neuropeptides, and the release of other secretions such as hormones, growth factors and cytokines. Each of the different types of chemical messenger can also influence the functioning of the brain and nervous systems.

THE CASCADE OF CHEMICAL MESSENGERS

As shown in Figure 4, there is a cascade of chemical messengers: a nerve cell releases a neurotransmitter which regulates the release of neurohormones from hypothalamic neurosecretory cells. These hypothalamic hormones stimulate the cells of the adenohypophysis to synthesize and release their hormones. Many of these pituitary hormones, such as LH and FSH, act on endocrine target cells, such as the gonads, causing them to synthesize and release their own hormones (estrogen and progesterone), which stimulate biochemical changes in target cells in the body or brain. In each step of this pathway the neurotransmitters and peptide hormones stimulate membrane receptors which activate a second messenger, such as cAMP, within the target cell. The steroid hormones act on receptors located inside the target cells.

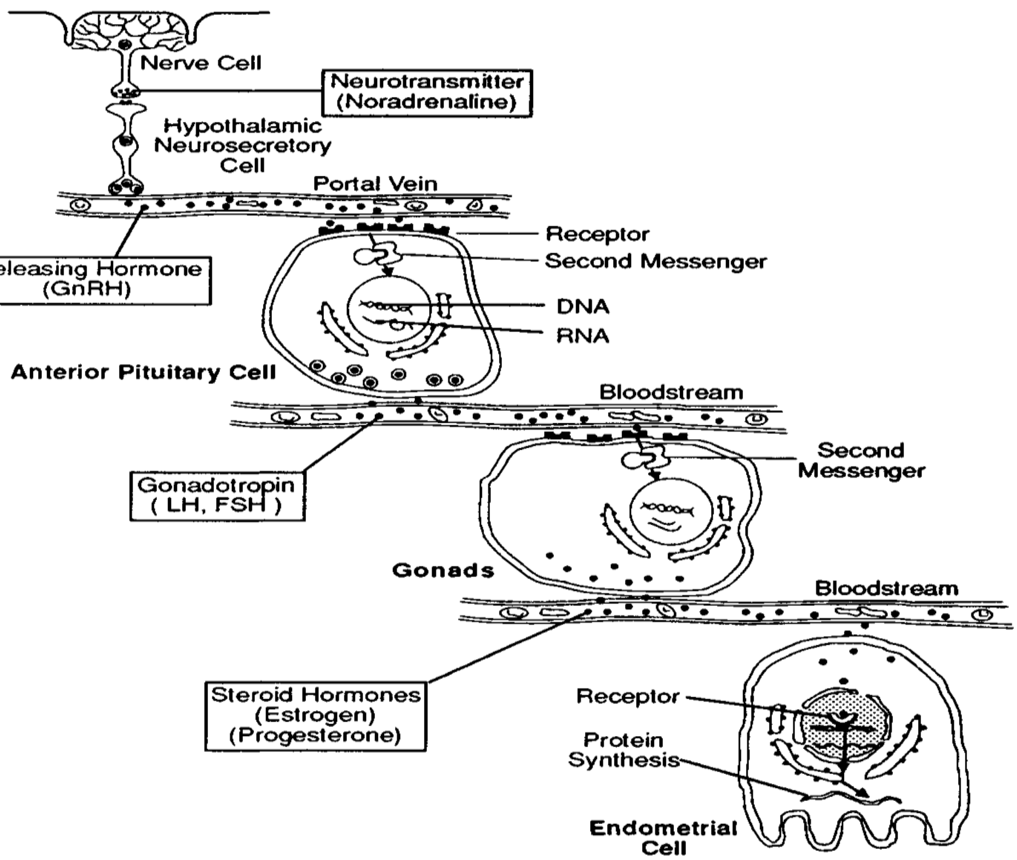

Fig 4: The cascade of chemical messengers through which neurotransmitters can regulate the neuroendocrine system. A neurotransmitter (perhaps noradrenaline) is released from a neuron and stimulates a hypothalamic neurosecretory cell to secrete a neurohormone, such as GnRH, into the hypophyseal portal veins, which transport it to the anterior pituitary, where it stimulates receptors on gonadotroph cells. These receptors activate a second messenger system within the cell which causes the synthesis and release of pituitary hormones, such as LH and FSH. These pituitary hormones enter the general circulation where they are picked up by receptors on their target cells in the gonads where they act, by way of the cAMP system, to stimulate the synthesis of the gonadal steroid hormones, estrogen and progesterone. The gonadal steroids move through the blood-stream to their target cells, some of which are in the endometrium of the uterus, where they interact with the cell nucleus via intracellular receptors to stimulate protein synthesis.