Functional Unity of the Immune, Endocrine and Nervous Systems

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Abstract:
Information on the functional relationship of the immune, endocrine and nervous systems of the body is presented, numerous evidences of this unity are presented, including the cross-activity of immunotropics and neurotransmitters, hormonal preparations, corresponding cell receptors, regulation of homeostasis by the coordinated action of these three systems, an integral biochemical mechanism, caused -giving the unity of systems, etc.

Logic dictates that the life support of the organism must be conditioned, at least by the functional unity of the most important (more precisely all) systems organism. Perhaps the unifying principle of this is the immune system. Let us recall how its definition changed: in 1955 - "protection of the organism from this or that infectious disease", in 1987 -"protection of the body from foreign information", recently - "immunity is disseminated the mobile brain, and the main character - the lymphocyte is a disconnected circulating gland".

Today, biological scientists are looking at the immune system as a comprehensive receptor organ that recognizes and sorts external and internal antigenic signals of different nature, transmits significant volume of information both on nerve fibers and through blood flow to strategically rationally located organs of the immune system, using numerous combinations of cellular and humoral factors involving hormones. The central nervous system, in turn, having received and processed the signal, renders influence by the type of feedback on the regulation of immune reactivity and hormonal background.

These systems have in common the general principles of functioning. So, the immune and nervous system: 1-cause specific reactions, dependent on the inducing effect, 2 -possess memory, i.e. change the nature of the response to repeated exposure to the factor, 3 -have a branched structure in the body that permeates all its structures, 4 -leading to a change in the functioning of other body systems. Indeed, for example, anaphylactic shock induced by a purely immune reaction (association of a specific antigen/allergen with an antibody), almost instantly causes the release of biogenic amines, which immediately is manifested by characteristic behavioral reactions for which the central nervous system and significant changes in the endocrine status. The opposite situation is also possible, when induction, for example, purely endocrine phenomena - hypoglycemic, hypothyroid, hypocorticoid com, accompanied by very specific reactions of the nervous and the immune systems.

The proof of this unity is the fact that the «left-handed» Individuals increased by 2.5 times the frequency of development of immune disorders, moreover, their children also have an increased risk of developing immunopathological conditions, even when they were right-handed.

Thus, the regulation of homeostasis is characterized by the simultaneous participation of various physiological reactions. Moreover, immune disorders associated with biochemical disorders, forming a single symptom complex of pathology, which is based on individual cells with impaired metabolism, located in various organs and tissues. It is clear that the clinic the disease is determined by the localization of the lesion and regulatory disorders mechanisms due to closely related immune, nervous and endocrine systems. The available data suggest that adequate correction of immune disorders is accompanied by the normalization of indicators biochemical and clinical status. In other words, immunotropic agents act not only on the immune system, but also carry out a general biological effect (1,2,3,4,5,6,7,8,9,10).

The authors provide a number of proofs.

(1) The ability of different parts of the brain to significantly and differentially influence immune responses. The special term "brain lateralization" has been developed. For example, the surgical destruction of the hypothalamus (anterior, lateral, tubular, or nipple region) leads to a violation of antimicrobial immunity, while the antiviral protection (T-cell immunity) does not suffer. The same results could be achieved with medication. Experimental or natural, for example, in malignant neoplasms, damage to the cortex of the right hemisphere leads to inhibition of the functional activity of T- lymphocytes, while left-sided damage does not cause such an effect.

(2) The established fact is the innervation of the organs of the immune system with a change in its function when nerves are damaged. The transection of the trunks that innervate the thymus or bone marrow leads to a modification of the immune response, which causes a violation of the integrity of the central nervous system, especially the hypothalamus. Sympathectomy is accompanied by changes in the cellular composition of the bone marrow, thymus, and spleen. With electrical stimulation of the hypo-thalamus or peripheral nerves, AT formation is enhanced. Damage in the area of the anterior hypothalamus reduces the killer effect of monocytes.

(3) The dependence of immune reactivity on conditionally reflex function of the central nervous system. There are known examples of the development of attacks of bronchial asthma and other manifestations of allergies when the patient enters the premises, where these reactions have developed in the past, even in the absence of a provoking factor - allergen. The opposite situations are also possible, in which the lines mice with the occurrence of autoimmune diseases were able to achieve recovery when developing a positive conditioned reflex to the drug means with its subsequent cancellation.

(4) There is growing evidence that intellectual memory has a direct connection with immunocompetent cells. In experiments treatment of subjects with monoclonal antibodies against certain structures of T- lymphocytes caused memory loss (amnesia) and loss of stable conditioned reflexes. Moreover, the severity of this process depended on the dose of antibodies used, which is possibly due to the fact that the specified the receptor is simultaneously presented on T and on nerve cells (see below).

(5) The immunocompetent sphere is capable of producing various regulatory peptide hormones: adrenocorticotropic (ACTH), thyrotropic (TTH), somatotropic (STH), arginine-vasopressin, oxytocin, neurophyzine, prolactin, vasoactive intestinal polypeptide. Monocytes, lymphocytes and splenic macrophages produce or stimulate the formation of ACTH, endorphins, γ-melanostimulating hormones, corticotropic a similar peptide. Bone marrow synthesizes met-enkephalin, β-endorfin, in the thymus leu- and meth-enkephalins, β-endorphins. Some populations plasma cells of the intestinal mucosa form an immunoreactive β-endorphin. Immunoreactive enkephalins and growth hormone are synthesized T- lymphocytes, especially after activation by staphylococcus toxin. Somatotropic hormone can be produced by stimulating T-and B - lymphocytes and macrophages, and vasoactive intestinal polypeptide - polymorphonuclear leukocytes, neutrophils, eosinophils, basophils. After treatment of T-and B-cells with mitogen, they produce a factor activating the growth of glia.

(6) Mediators have a pronounced "endocrine-like" effect the immune system. So, α- and β-interferons are able to reproduce endocrine function, for example, in adrenal tissue culture to induce synthesis of corticosteroids, like ACTH, like melanotropin determine the synthesis of melanin, thyroxine, increase the binding of iodine by cells the thyroid gland, like glucagon, suppress insulin activity. The neurotropic effects of α-interferon are manifested in its excitatory action on neurons. The ability of IL-1 through the hypothalamus is known to modulate the secretion of endorphins and thereby regulate the level of ACTH in the blood, corticosterone, glucose. Classic mediators of the immune response have relation to neuroendocrine regulation. Thus, IL-2 stimulates proliferation, differentiation of oligodendrocytes, excites the reactivity of neurons hypothalamus, regulates gene expression in pituitary cells, increases blood levels of ACTH and cortisone. α-

tumor necrosis factor with internal intraventricular injection into the brain increases the pain threshold and suppresses locomotor activity.

Known neurotropic effects of myelopeptides (11) with the preservation of the endorphin effect for 1.5 hours. IL-1 acts on liver function by influencing the synthesis of serum amyloid A, CRP, C3-complement component, α-tumor necrosis factor, chymotrypsin, albumin, transferrin.

(7) Mediators of the immune system can be formed in the cells of the central nervous system: interferon, interleukins, tumor necrosis factor, thymic peptides. For example, cells of the cerebral cortex when damaged by viruses and autoimmune processes produce IL-2, and interferon and IL-1 are synthesized as astrocytes and glial cells. Follicle-dependent cells of the anterior lobe the pituitary gland, outwardly similar to mononuclear phagocytes, produce IL-6. Nerve tumor necrosis α-factor promotes migration granulocytes in the central nervous system and stimulates the production of 0_2-radicals in them. Thus, signals from the immunocompetent sphere can be transported to the central nervous system and higher departments of neuroendocrine regulation and vice versa using traditional immune response mediators.

(8) Nerve and immunocompetent cells have common receptors. Thymus and cerebral cortex cells have a common Thy-1 antigen. Identical receptors for vasoactive intestinal polypeptide isolated from lymphocytes and brain cells. They are similar to opioid receptors derived from lymphocytes and nerve cells, receptors to the growth release factor from pituitary cells, thymic lymphocytes, spleen, and bone marrow. There are common receptors for interferon and IL-2 on brain and lymphoid cells. On lymphocytes and monocytes/macrophages there are also receptors for glucocorticosteroids, insulin, STH, neurotransmitters, acetylcholine, β-adrenergic agents, through which metabolism, transport of various substrates, allosteric membrane changes, lymphoid cell proliferation, synthesis monokines. Activated monocytes/macrophages and lymphocytes are able to be stimulated via lymphokines and other mediators of the adrenal cortex. On the other hand, receptors capable of binding to antigens have been found on non-lymphoid elements, for example, in myocardial cells, which somewhat dilutes the exclusiveness of immune responses (12).

(9) The immunotropic effects of hormones are known. Thus, the pituitary hormone ACTH is endowed with an immunosuppressive effect due to inhibition of the production of γ-interferon. STH, on the contrary, stimulates immunity, especially its cellular link, enhances proliferation in the thymus, spleen, lymph nodes, activates the precursors of T-lymphocytes, NK-cells, bactericidal activity of macrophages.

Neurohypophyseal hormones - oxytocin, vasopressin intensify antibody synthesis and phagocytosis.

Thyroid stimulating hormones have immunostimulating properties. Thyroxine, triiodothyronine increase the functional activity of B-cells, antibody formation. Calcitonin, which is one of the thyroid hormones is able to stimulate rosette formation of cells of the spleen, thymus and bone marrow.

The pineal gland hormone melatonin potentiates the formation of antibody-forming cells.

The parathyroid hormone (parathormone) reduces the proliferativelymphocyte activity and colony-forming ability of bone cells brain.

Sex hormones - estrogens in low doses stimulate, in high doses they inhibit mitoses in immunocompetent cells, reduce their response to PHA, suppress activity of NK-cells, inhibit the function of T-suppressors. Action of androgens on the immune system in different directions. Testosterone in different conditions can reduce or increase humoral immunity, while proliferating activity of T-cells does not change. This hormone can change differentiation of stem cells towards erythropoiesis to the detriment of formation lymphoid elements. Chorionic gonadotropin in low concentrations oppresses, in large - potentiates the formation of antibodyforming cells.

In general, the activity of lymphoid cells under physiological conditions is influenced by inhibitory effect of adrenal hormones and sex steroids, stimulating by hormones of the thyroid, pancreas and pineal gland.

(10) There is a biochemical mechanism that determines the unity of the three systems - these are the cyclic nucleotides cAMP and cGMP. It is known that 3,5'-AMP inhibits the reaction of phagocytosis in neutrophils, proliferation and differentiation of lymphocytes, T- and B- effector cells, cellular and humoral responses to antigens. At the same time, 3,5'-GMF stimulates these processes. On the other hand, the association of cyclic nucleotides with the endocrine system was found. Thus, the hormones of the anterior pituitary gland - ACTH, STH, luteinizing cause in the adrenal cortex, thyroid gland, ovaries, an increase in the activity of adenylate cyclase and the accumulation of cAMP. The action of the hormones of the posterior and middle lobe of the pituitary gland - vasopressin, oxytocin and melanostimulating hormone is mediated through cGMP. Hormones of the parathyroid glands - parathyroid hormone and calcitonin change the content of cAMP in cells. Glucagon, synthesized in the pancreas, has a stimulating effect on glycogenolysis, lipolysis, gluconeogenesis through 3,5'-AMP. According to the latest data, sex steroid hormones also depend on the system of cyclic nucleotides.

For adrenergic mediators, cAMP acts as a secondary messenger, for cholinergic cGMP plays a similar role. On the other hand, the response of nerve cells to synaptic stimulation by neuromediators, manifested in a selective change in the permeability of the synaptic membrane to specific ions, is also due to cyclic nucleotides.

(11) Low molecular weight nucleic acid fragments, and, first of all, RNA, are also capable of influencing the functioning of the analyzed systems. Note that these regulators are constantly present in the body, entering the internal environment with food and, as a result, physiological and pathological cell destruction. It is known that the general biological, rather than genetic, effect of nucleic acids, which is expressed in a powerful modulating effect on immune responses, is capable of changing the formation of endogenous corticosteroids, possibly other hormones, realizing an analgesic effect, promoting the regeneration of damaged nerve cells, restoring lost memory in the elderly. Finally, they modulate the cAMP/cGMP system.

Thus, regulatory peptides of the immune system are able to influence to determine the functional parameters of somatosensory cells and vice versa. Therefore, various pathological processes can simultaneously cause disorders of all three systems. At the same time, the correction of violations of one of them, for example, the immune, entails changes in the organismic character, which is expressed in changes in the endocrine status, functioning of the nervous system, metabolic parameters, etc.

References

i. Zdrodovsky PF. Infection, Immunity and Allergy problems, Publishing House: Medicina, Moscow, 1969: 462p.

ii. Zemskov MV, Sokolov MI, Zemskov VM. Fundamentals of General Microbiology, Virology and Immunology, Publishing House: Kolos, Moscow, 1977: 271p.

iii. Ketlinsky SA, Simbircev AC, Vorobyov AA. Endogenous Immunomodulators. Publishing House: Hippocrates, St. Petersburg, 1992: 256p.

iv. Korneva EA. Modern Aspects of Studying the Problem of Neuroimmunomodulation. Russian J of Immunology, 1999, Vol-4, Issue-1F: 305-308.

v. Senyuk OF, Skorobogatenko OV, Tarasenko PD. Ceruloplasmin Protects the Erythrocyte Membrane. Biochemistry, 1998, Vol-63, Issue-12: 1691-1694.

vi. Akmaev IG. Neuro-immuno-endocrinology: Facts and Hypotheses, Endocrinology Problems,1997, Issue-1: 3- 9.

vii. Zemskov VM, Neymann VV, Pronko KN, Zemskov AM. Global Role of Low Molecular Weight Nucleic Acids in Biological Systems. Global J Med Res, 2020, Vol-20, Issue-2: 5-10.

viii. Zemskov V, Pronko K, Zemskov A, Zemskova V. Complexity Problem in Immunology, Australasian Med J, 2018, Vol-1, Issue-9: 465-473.

ix. Zemskov AM, Zemskov VM, Chereshnev VA (Ed.). Encyclopedia of Immunology in 5 volumes. Publishing House: Triada-X, Moscow. 2013: 1962p.

x. Zemskov AM, Zemskov VM, Donzov AV, Donzova EV, Zemskova VA, Redkin AN. Metabolic Syndrome as a Homeostasis Modification Factor. International Journal of Current Advanced Research, 2017, Vol-6; Issue-1: 1640-1644.

xi. Petrov RV, Khaitov RM, Manko VM, Mikhailova AA. Control and Regulation of the Immune Response. Publishing House: Medicina, Moscow, 1981: 375p.

xii. Kulberg AYa, Berkun YB. Serum IgG as a Lectin Inhibitor: A New Approach to Studying the Functional Interaction of Natural and Acquired Immunity Factors. Immunology, 1998, Issue-1: 7-10.