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BRAIN AND ADAPTIVE MECHANISMS OF THE ORGANISM — INTRODUCTION

Physiology is a branch of science dealing with the mechanisms of functioning of living organisms. All environmental factors trigger functional changes of organs and entire organisms. Mechanisms assuring a coordinated action of different organs are of primary importance for the functioning of animals (especially vertebrates and man) and for their survival in a changing environment. Complex adaptive changes, expressed at the molecular level but also in the organism's behavior, would have been impossible without the participation of three systems: nervous, endocrine and immunological. The nervous system is characterized by an exceptional variety of integrative functions at all levels of biological organization. The papers assembled in this issue of *Kosmos* are intended to display the abundance of mechanisms with which the nervous system assures the integration of adaptive changes occurring in the organism.

Excitability and plasticity are two major features of the nervous system. Plasticity means the ability to undergo lasting functional and structural changes due to the processed information. The discovery of various carriers of the cell to cell information has greatly enriched the understanding of regulatory mechanisms, not only on the cellular but also on the organismal level. Striving for a global view of the basic adaptive reactions of animal organisms is probably the most important feature of contemporary neurobiology — that branch of science gradually fills the place traditionally occupied by neurophysiology. Most of the papers collected in this issue have such an neurobiological character.

The last ten or so years have witnessed a very massive infiltration of molecular biology into most branches of physiology. The paper *Developmental plasticity of the nervous system* by M. Kossut is a good introduction to these problems. The phenomena of developmental plasticity are illustrated by data coming from classical experimental models and by her own data on representations of whiskers in the brain somatosensory cortex. The reader is presented with a number of facts concerning overproduction of cellular elements in the nervous system, the genetically programmed cell death and meaning of the so called critical periods in development. All these phenomena are discussed in terms of the significant

influence of epigenetic factors on genetically determined developmental processes. This influence enables the nervous system to get attuned to conditions imposed by the environment. The general view on the development of several highly specialized brain structures, presented in the paper, might be of interest for specialists from different fields of biology.

Studies on the nervous system development proved that diffusible factors produced by various cells could serve not only as chemical markers enabling the growing axons to reach specific target structures, but could also assure neuronal survival (hence their general name — neurotrophins). The paper by A. Bacia, W. Jegliński and B. Oderfeld-Nowak entitled *Role of the nerve growth factor in brain* presents the history of discovery and the mechanisms of functioning of the best known neurotrophin, the nerve growth factor (NGF). The mechanism of action of endogenous NGF on the cholinergic neurons and of exogenous NGF on the noncholinergic neurons is presented in the studies using models of brain injury and brains of old animals. A hypothesis linking degenerative changes of neurons observed in neurological diseases of old age with decreased availability of neurotrophic factors is presented.

The carriers of information between the cells, that is neurotransmitters, neuropeptides and neurotrophins and other neuromodulators, reach the specific receptors on the neuronal membrane and activate various processes inside the neuron. The paper by I. Figiel and L. Kaczmarek *Second messengers in neuronal plasticity* describes the main pathways of information transfer inside the nervous cell. Particular attention is paid to molecular tools enabling the integration of information from different sources. The importance of such "coincidence detectors" is described in several well investigated models of neuronal plasticity. The signal received by the membrane receptors reaches also the cell nucleus and can cause the activation of specific genes. A. Goc in the paper *Molecular mechanisms of plasticity of chromaffin cells* describes the mechanisms of information reception by regulatory elements inside the genes. Some stimuli which disturb the organisms' homeostasis cause a long-lasting activation of adrenal chromaffin cells, greatly outlasting the duration of the stimulus. Activation of these specialized cells is manifested by increased synthesis of catecholamines and neuropeptides. The intensity of catecholamine synthesis depends on the activity of tyrosine hydroxylase, and the long lasting changes of functioning of chromaffin cells are linked with the activation of this enzyme's gene.

While the functional and anatomical links between the nervous and endocrine systems are well known, the studies of interactions between the nervous and immunological systems reached momentum only recently. The paper *Integrity of the nervous and immune systems* by A. Skowron-Cendrzak presents new data in this field. Attention is attracted to local immune reactions in the brain — the organ privileged in this respect, protected by the blood-brain barrier, the organ containing a negligible amount of classic elements of the immunological system. Also of

interest is the chapter describing the transmission of signals between the nervous and endocrine systems by adrenergic fibers, but mainly by a rich array of hormones, neuropeptides and cytokines.

All the above-mentioned papers give numerous examples of the importance of various chemical messengers for the functioning of the nervous system and its integration with other systems. The paper by W. Turski and Z. Kleinrok: *Excitatory amino acids in synaptic transmission* concerns one compound, glutamic acid, the main excitatory neurotransmitter. Different subtypes of ionotropic and metabotropic receptors of excitatory amino acids are described, as well as agonists and antagonists binding to the regulatory sites of these receptors. A hypothesis on the mechanism of neuronal degeneration resulting from prolonged exposures to high concentrations of excitatory amino acids, is presented together with the possibility of therapeutic application of their antagonists.

The main topic of the paper by J. Maj entitled *Neuropsychopharmacology — achievements and prospects* is the analysis of neuropsychotropic drugs as tools for studying the basic neuronal processes such as biosynthesis and release, degradation and neuronal uptake of mediators. The knowledge of theses processes is important for studies of the organization of the central nervous system. The chapters about serotonin and neuropeptides well illustrate the possibilities offered to the investigator by a drug that often causes effects and states of organism not attainable in any other way. The paper describes in a synthetic way several problems discussed during the annual Winter Schools of Pharmacology in Mogilany, organized by the Institute of Pharmacology of the Polish Academy of Sciences.

Circulating blood removes from the brain, together with the metabolic products, the metabolic heat, generated in considerable excess. The raise in brain temperature above a certain threshold, much lower for the brain than for other organs, causes severe disturbances of neuronal structure and function. The paper by M. Caputa *Why does our face show signs of our feelings? Thermoregulation of the brain* demonstrates that the brain is privileged with respect to thermoregulation, just as it is in the case of immunological reactions. Different mammalian species have very efficient ways of selective cooling of the brain. At the same time, subtle changes of brain temperature linked to emotional states are observed. EEG arousal and behavioral activation lead to changes of neuronal activity of the amygdala and the motor cortex caused solely by the increase in temperature of these structures — important centers for evaluation of a situation and initiation of the organism's reaction.

The limbic system is the center of emotions and the main link of controlling even the most elementary forms of behavior: seeking food, water, shelter, mates, and avoiding harmful stimuli. Several papers analyze various aspects of functioning of the limbic system and its constituent structures. W. Trojniar in her paper *Physiological mechanism of reward* elaborates the thesis that the organism's activity is primarily dependent upon evaluation of the emotional content of

environmental stimuli, upon their rewarding and motivational role. She describes experimental models in which the rewarding value of stimuli can be measured and analyzes the experimental results showing that the mesencephalic dopaminergic system is an important link in the mechanism of reward. Elucidation of the functional mechanisms of the reward system can lead to finding of effective therapeutic methods for such disorders as obesity, alcoholism, drug addiction etc.

The paper *The amygdala — a sensory and motivational integrator* by T. Werka is concerned mostly with associative functions of this limbic structure. The author's results concerning the transfer of avoidance reaction and post-stress analgesia prove the important role of the amygdala in processing the motivational aspect of sensory information. The analysis of anatomical structure of the amygdaloid body, the connections of different nuclei and, first of all, the results of selective lesions, suggest that the amygdala, during the transformation and transfer of sensory information from the environment, significantly influences the processes of regulation of motivational states and in this way regulates the adaptive reactions of the organism.

The paper *Organization of the frontal lobe association cortex in brain* by A. Kosmal is devoted to structural and functional differentiation of the highest level of the nervous system. The basic scheme of cortical architecture is presented for the dog and monkey brain. During evolution, significant changes occurred in the short distance connections between adjacent cortical fields as well as in "associative" connections between distant cortical fields. A characteristic feature of the primate brain is the high degree of convergence in several small cortical regions — the multimodal areas. These areas are interconnected by bilateral long associative connections, while at the same time they retain strong links with the limbic structures and the motor cortex. The author's own results suggest that, in the *Carnivora*, the beginnings of convergence of various sensory systems appear in the dorsal zone of association cortex of the frontal lobe.

A reflex is a functional unit of the nervous system, permitting the organism's reaction to external and internal stimuli. Several reflexes are genetically determined; others are acquired. The reflexes acquired during ontogenesis make possible proper evaluation of meaning of different environmental stimuli and utilization of the learned relations between stimuli and the organism's reactions. The paper by K. Zieliński entitled *Conditioning and association formation* presents a thesis that the matching of stimuli and events closely spaced in time and space is the basis for formation of associations, while formation of conditioned reactions requires additionally the evaluation of probability of occurrence of certain events.

The last four papers deal with the consequences of brain function impairment by ageing and diseases. O. Narkiewicz and J. Moryś in their paper entitled *Hippocampus and memory deficits in Alzheimer's disease and ageing* describe the history of research on the function of the hippocampus — the brain structure which, because of its cytoarchitecture, anatomical connections and functional importance,

attracts many scientists. The authors stress the differences in memory impairments due to slowing down of the psychic processes in old age and memory deficits caused by pathological changes. In the paper *Postural stability control* by J. Błaszczyk the comparisons between young and elderly persons demonstrate the variety of strategies used for regulation of body posture in man. The inclined body position and the strategy of slow movements of smaller amplitude, observed in older subjects, are adaptive strategies allowing the preservation of motor activity when the neural mechanisms controlling posture are weakened. In several papers describing dopamine, the neurotransmitter produced by substantia nigra and acting on neurones in the striatum, Parkinson's disease was mentioned as an example of disturbance within this system. The paper by A. Friedman — *Parkinson's disease — facts, opinions, hypotheses*, which analyzes the data concerning the etiology of this disease, illustrates the long way leading from the discovery of basic biochemical processes to the understanding of causes of the disease.

The last paper of this issue is *Kindling — a concept of pathogenesis of some neurological and psychiatric disorders* by J. Majkowski. Kindling is an increase of neuronal reactivity as a result of weak, repeated at long intervals, electrical, chemical or sensory stimulation of a restricted brain site. Local changes evoked by this kind of stimulation often lead to the appearance of an epileptic focus. The author's attention is, however, directed mostly to the generalized changes, leading to lasting changes in bioelectrical and behavioral reactions. Observations of the progressive character of both the epileptic focus and the psychoses are the basis for formulating the hypothesis about preservation of abnormal activity of the brain.

All the above papers do not give a full review of the mechanisms which permit the brain to coordinate and integrate different adaptive reactions of the organism. They are, however, a good illustration of the change in research interests of neurophysiologists that occurs in front of us. To keep pace with the trends of the world's science, about ten years ago an effort was undertaken in Poland to study biochemical and physiological mechanisms of cellular interactions, as a basis of functioning of more complex systems, particularly the brain — the most complex system created in the process of evolution. Most of the authors who were willing to sacrifice their time and write the review papers for this issue, participated in the above-mentioned research effort, organized and coordinated by The Nencki Institute which celebrates its 75th anniversary this year.

Comprehensive research oriented to clinical needs is the essence of "The Decade of the Brain", an unprecedented scientific and organizational enterprise started 3 years ago. The reason of popular support for concentrated brain research lies in the challenges of contemporary civilization. Brain diseases and impairments are one of its major threats. Numerous scientific organizations led by the International Brain Research Organization and governmental agencies of several countries have joined the initiative of the Congress of United States of America. In the resolution adopted by the General Assembly of the Polish Academy of Sciences

on December 6th 1991 and directed to the Parliament of the Polish Republic with an appeal to join the "Decade of the Brain", we find these lines:

"Brain, as the most perfect investigative and creative tool, the site of mental and emotional activity of man and the most effective biological regulatory system, is facing the challenge of understanding itself. The development of biology and molecular pathology, the knowledge of signal transmission and intracellular interactions, as well as the mechanisms of memory and regulation of emotions, have made it possible to undertake this challenge."

This appeal of Polish scientists was left unanswered by the ruling bodies of our country. The present collection of review papers is another proof that Poland is capable of preparing and implementing a multidisciplinary research program, which would contribute to the worldwide effort.

I want to thank all the authors for their participation in elaborating the concept of this issue and for their effort in its creation. I also thank my colleagues, particularly Leszek Kaczmarek, Olgierd Narkiewicz, Jan Ryżewski and Bogusław Żernicki for participation in editorial work and for help with terminology.