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Developing brain as an endocrine organ: A paradoxical reality

Michael V Ugrumov
Institute of Developmental Biology, Russia

The maintaining of homeostasis in the organism in response to a variable environment is provided by the highly hierarchic neuroendocrine-immune system. The crucial component of this system is the hypothalamus providing the endocrine regulation of key peripheral organs, and the adenohypophysis. In this case, neuronderived signaling molecules (SM) are delivered to the blood vessels in hypothalamic "neurohaemal organs" lacking the blood–brain barrier (BBB), the posterior lobe of the pituitary and the median eminence. The release of SM to the blood vessels in most other brain regions is prohibited by BBB. According to the conventional concept, the development of the neuroendocrine system in ontogenesis begins with the "maturation" of peripheral endocrine glands which first are self-governed and then operate under the adenohypophysial control. Meantime, the brain maturation is under the control of SM secreted by endocrine glands of the developing organism and coming from the placenta and maternal organism. The hypothalamus is involved in the neuroendocrine regulation only after its full maturation that is followed by the conversion of the opened-looped neuroendocrine system to the closed-looped system as in adulthood. Neurons of the developing brain begin to secrete SM shortly after their origin and long before the establishment of specific interneuronal relations providing initially autocrine and paracrine morphogenetic influence on differentiating target neurons. Taking into account that the brain lacks BBB over this ontogenetic period, we hypothesized that it operates as the multipotent endocrine gland secreting SM to the general circulation and thereby providing the endocrine regulation of peripheral organs and the brain. The term "multipotent" means that the spectrum of the brain-derived circulating SM and their occupancy at the periphery in the developing organism should greatly exceed those in adulthood. In order to test this hypothesis, gonadotropin-releasing hormone (GnRH), dopamine (DA), and serotonin (5-hydroxytryptamine, 5-HT) were chosen as the markers of the presumptive endocrine function of the brain in ontogenesis. According to our data, the concentrations of GnRH, DA, and 5-HT in the rat general circulation during the perinatal period, i.e. before the establishment of BBB, was as high as those in the portal circulation in adulthood. The concentrations of circulating GnRH and DA dropped to almost undetectable level after the development of BBB suggesting their brain origin. This suggestion has been proven by showing an essential decrease of GnRH, DA, and 5-HT concentrations in general circulation of perinatal rats after microsurgical elimination of synthesizing neurons or the inhibition of specific syntheses in the brain before the establishment of BBB. GnRH, DA, and 5-HT apparently as dozens of other brain-derived SM appear to be capable of providing the endocrine influence on their peripheral targets like the adenohypophysis, gonads, kidney, heart, blood vessels, and the brain (endocrine autoregulation). Although the ontogenetic period of the brain operation as the multipotent endocrine gland is relatively short, the brain-derived SM are thought to be capable of providing long-lasting morphogenetic effects on peripheral targets and the brain. Thus, the developing brain operates as the multipotent endocrine gland from the onset of neurogenesis to the establishment of BBB providing the endocrine regulation of the developing organism.

Biography

M Ugrumov graduated from Moscow University Medical School in 1970 and received PhD at Institute of Evolutionary Physiology and Biochemistry USSR Academy of Sciences in 1974. He was a Senior Researcher at the Institute of Human Morphology RAMS (1974-77) and the Institute of Developmental Biology RAS (1977-87). He is a Head of the Laboratory at the Institute of Developmental Biology from 1987 and at the Institute of Normal Physiology from 1996 till now. He got a Professorship in Pharmacology and Radiobiology in 1996 at the State Medical University, Moscow, Russia and elected as a Corresponding Member of the Russian Academy of Sciences in 1997 and as a full Academician of the Russian Academy of Sciences in 2006. He is the advisor to the President of the Russian Academy of Sciences (RAS) on International Scientific Cooperation, a member of the Scientific-technical Council at Chairman of the Federal Assembly of RF, Vice-president of Russian Physiological Society. He was a Visiting Prof. at: Univ. Medical School, Tokushima (Japan) in 1988-89; Medical University of Ulm (Germany) in 1993; University of Tours (France) in 1998, 2000; University P. et M. Curie (Paris, France) in 1993-2010.

mugrumov@mail.ru