New model to explain the role of dopamine in immune regulation described

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Dopamine is a neurotransmitter that is associated with emotions, movement, and the brain's pleasure and reward system. In the current issue of *Advances in Neuroimmune Biology*, investigators provide a broad overview of the direct and indirect role of dopamine in modulating the immune system and discuss how recent research has opened up new possibilities for treating diseases such as Parkinson's and Alzheimer's disease, schizophrenia, multiple sclerosis or even the autoimmune disorders.

Dopamine can be synthesized not only in neurons, but also in immune cells which orchestrate the body's response to infection or malignancy. "Data strongly supports the theory that an autocrine/paracrine regulatory loop exists in lymphocytes, where dopamine produced and released by the cells then acts on its own receptors, and can have an influence on its own function," explains lead investigator György M. Nagy, PhD, DSc, of the Department of Human Morphology, Cellular and Molecular Neuroendocrine Research Laboratory, Hungarian Academy of Sciences, and Semmelweis University, Budapest, Hungary.

Elements of dopamine signaling and metabolites can also serve as a communication interface between the central nervous system and immune system, and that communication can work in both directions. Lymphocytes that can pass the blood brain barrier can be "educated" by locally secreted neurotransmitters, including dopamine. Then they transmit brain-driven messages to other cells of the immune system via direct or indirect pathways.

Permanent dysfunctions of either the central (CNS) or the peripheral (immune) dopaminergic system are frequently associated with immune malfunctions. Current dopamine replacement or receptor blocking therapies are based on the supposed action of these drugs at the target site, and they often only relieve disease symptoms. The mainstream in design of new therapies is to find drugs having more-and-more specific action and minimal or no potential side effects, however, there is always a risk/benefits consideration in the drug development processes. These approaches may need to be revisited with the concepts of neuroimmunomodulatory influence, and focus on the cross-talk between the immune and nervous systems," Dr. Nagy says.

Various immune mechanisms may contribute to the pathogenesis of neurological disorders. The pharmacological design of targeted drug delivery systems could carry a desired compound right to the sites of cellular pathologies, Dr. Nagy observes. "Well designed clinical trials are needed for the critical evaluation of the new theories in human therapy, either by the use of available drugs with extended immunomodulatory functions, or newly designed compounds, or the combination of both. Evaluation of clinical efficacy and data on safety of patients should provide an answer to these questions," he concludes.

In a commentary accompanying the article, Istvan Berczi and Toshihiko Katafuchi, Editors-in-Chief of *Advances in Neuroimmune Biology*, ask why a central nervous system mediator such as dopamine would be produced locally, when dopamine made centrally could be deployed when necessary. "We suggest that the function of paracrine/autocrine (P/A) circuits is to maintain tissue viability in emergency situations, when no other regulators are available. Local P/A circuits are the key to healing and recovery," they say.

Dr. Berczi and Prof. Katafuchi note that the science of cryobiology, which deals with the medical application of hypothermia and freezing

and tissue culture techniques, which grow cells and tissues in vitro from animals and man, owe their existence to P/A circuits to preserve tissue viability and reactivity beyond clinical death or under proper culture conditions. "Clearly, P/A circuits hold the possibility of resurrection after clinical death," they conclude.

More information: "Role of Peripheral and Brain-Derived Dopamine (DA) in Immune Regulation," by B.E. Tóth, M. Vecsernyés, T. Zelles, K. Kádár, G.M. Nagy. DOI 10.3233/NIB-2012-012044 "Dopamine in Immunoregulation," by I. Berczi, and T. Katafuchi. DOI 10.3233/NIB-2012-012046 Advances in Neuroimmune Biology, Volume 3, Issue 2 (October 2012)

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