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Nenad Mitić, editor

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Book of abstracts

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Mathematical Modeling of the Hypothalamic-Pituitary-Adrenal Axis Dynamics in Rats

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Abstract

The hypothalamic-pituitary-adrenal (HPA) axis is a dynamic regulatory network of biochemical reactions that integrates and synchronizes the nervous and the endocrine systems functions at the organism level. In order to describe how this vast network of biochemical interactions operates, we have developed a nonlinear eleven-dimensional stoichiometric model that concisely describes key biochemical transformations that comprise the HPA axis in rats. In a stoichiometric model of a biochemical system, the outcomes of complex biochemical pathways are succinctly described by stoichiometric relations. In this representation, substances that initiate, i.e. enter a pathway are regarded to behave as reactants; substances that are generated in a pathway are regarded to behave as products; and the rates at which products of a pathway appear are jointly proportional to the concentrations of the reactants. In order to derive rate constants for specific biochemical reaction pathways, we have resorted to our recently developed nonlinear reaction model that concisely describes biochemical transformations in the HPA axis in humans. In this way, a mathematical framework is developed to describe in the form of a system of ordinary differential equations (ODEs) the integration of biochemical pathways that constitute the HPA axis on chemical kinetics basis. This, in turn, allows us to use numerical simulations to investigate how the underlying biochemical pathways are intertwined to give an integral HPA axis response at the organism level to a variety of external or internal perturbators of the HPA dynamics. Given that the HPA axis is a nonlinear dynamical network, its response is complex and often cannot be intuitively predicted, stoichiometric modeling can be harnessed for gaining additional insights into dynamical functioning of this complex neuroendocrine system.

Keywords: Hypothalamic-pituitary-adrenal (HPA) axis, rats, nonlinear dynamical network, system of ordinary differential equations