From Apelin, Ang II and AVP to Boolean Model of Central Regulation of BP.

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***Abstract*—**

I. Introduction

Central nervous system (CNS) regulates blood pressure (BP) via neurohumoral pathway in mechanism of long- and short-term regulation. Maintenance of resting BP levels is based on multiple feedback loops. Cardiovascular response to stress includes rather feedforwards projections from visceral and central receptors to signal-integrative regions, mainly in medulla oblongata, and to neurosecretory parts of the brain. Up to date, majority of computational models focus on peripheral factors as the renin-angiotensin system (RAS) and on maintenance of the body fluid homeostasis [1].

The purpose of the present study was to create a parametric model of centrally interacting peptides of angiotensin II (Ang II) and apelin (AP) in regulation of BP via release of vasopressin (AVP). Calculations were performed by means of MATLAB environment and were implemented in Python (ver. 2.6) programming language with Numpy (ver 1.5.1).

II. Experiments

Baseline mean arterial blood pressure (MABP) was modeled by a 72-order autoregressive (AR) model, calculated on the basis of direct measurement of MABP in conscious, normotensive WKY rats (n=14). High order of the AR model was confirmed by AIC and FPE criterions. The measurement of BP in WKY constitutes a part of experiment performed in Chair and Department of Experimental and Clinical Physiology of the Medical University of Warsaw [2]. Quantitative data referring to the AVP, AP and Ang II actions were collected from experimental analyses published since 1970. For the benefit of the computations, interactions between petides, BP and AVP levels were fitted by a B-spline, exponential and linear regression functions. Brain AP and Ang II were considered as a two compartments regulating AVP release via change in activity of paraventricular (PVN) and supraoptic nucleus (SON) of hypothalamus (Fig. 1).

Present model includes dose-dependent effects of peptides, and nonlinear effects of Ang II and AP on secretion of AVP. The model also includes the supraphysiological levels of plasma Ang II and AP.

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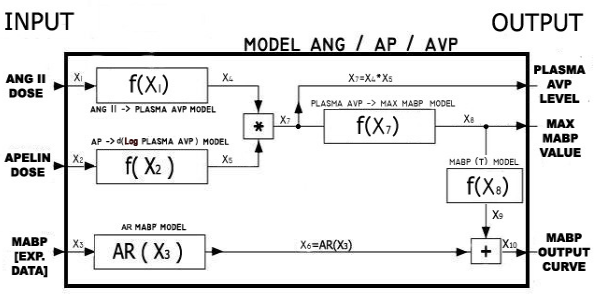

Figure 1. Blood pressure regulation model via Ang II/ Apelin/ AVP interaction

III. Models

Interactions described above are the part of a complex model that includes: the neuronal and secretory actions from hypophysis (PVN, SON), vasoconstrictor effect of AVP, feedback interactions from baroreceptors, actions of superior, caudal, rostral ventral and intermedial sites of medulla oblongata (NTS, CVLM, RVLM, IML), and regions sensitive to changes in blood osmolality and Na^+ concentration: area postrema (ArPo) and anterior ventral 3rd ventricle region (AV3V; SFO, OVLT, MnPO). Basis of the new approach was described by Boolean algebra and held in logic circuits simulation [3] (Fig. 2).

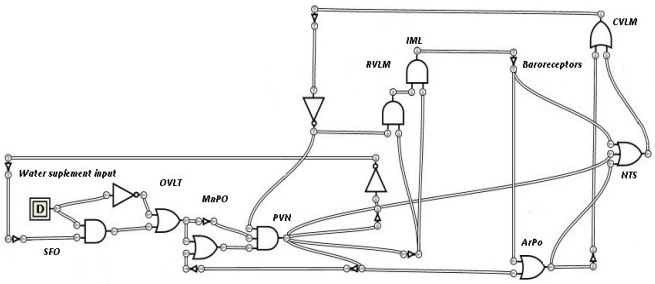

Figure 2. Foundamental model of centrally mediated blood pressure regulation described by logic circuit diagram.

References

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