

# Genetic modification of the paraventricular nucleus of the hypothalamus (PVN) to control hypertension chronically

Matos, TR.

Unidade de Sistema Nervoso Autônomo (IMM)  
[tiagoreismatos@gmail.com](mailto:tiagoreismatos@gmail.com)

**Background:** Persistent hypertension is one of the risk factors for strokes, heart attacks, heart failure and arterial aneurysm, and is a leading cause of chronic renal failure (...). In 95% of the patients, the cause remains unidentified and treatments typically only return arterial pressure to normal levels in one third of patients. It's known that the sympathetic nerve activity participates in the development and maintenance of elevated pressure values. Stimulation of paraventricular nucleus of the hypothalamus (PVN) is sympathoexcitatory and a pressure effect is mediated via direct and indirect (via the rostroventrolateral medulla) projections to the spinal cord. The PVN becomes more active under conditions of hypertension such as in the spontaneous hypertensive rats (SHR) model. A possibility of chronic manipulation of PVN neurons is expressing a human inwardly rectifying potassium channel (hKir2.1) under the control of the synapse promoter (a neuron specific promoter). In addition, it has an important role in determining the resting potential of the cell and plays a pivotal role in regulation of neural excitability.

**Objectives:** The proposed project was aimed to clarify the role of PVN cells on the essential hypertension as well as to generate data that could be useful in the development of therapeutics methodologies to treat essential hypertension. Through decreasing chronically the activity of the PVN neurons in SHR and in normotensive rats (Wistar) and record by telemetry the blood pressure and heart rate for analyze of sympathetic efferences by means of wavelets and spectra analysis.

**Methods:** A microinjection with a lentiviral vector is done on the PVN of the rats, and since they will integrate within the nucleus, it will cause chronic expression over months. Then the evaluation of autonomic sympathetic activity in chronic experiments involves the recording of variables like Heart Rate (HR) and Blood Pressure (BP) that can be done by telemetry. Not only are the absolute values of HR and BP sympathetic activity important but also the analysis of this variability in the time-frequency domain. Such analysis allows the definition of two bands, Low Frequencie (LF) and High Frequencie (HF), related to sympathetic and parasympathetic activity, respectively.

**Results:** There were significant differences on the systolic arterial pressure, diastolic arterial pressure, mean of the arterial pressure, HR and on the relation between the LF and the HF when comparing before and after the lentiviral vector injection. In the control cases, there were no significant differences before and after the injection on those criteria. The analyze of the values of the weight, food intake, water intake, faeces production and urine of the rats housed in metabolic cages before and after the injection of lentiviral vector or the sodium chloride solution was considered not significant.

**Conclusions:** The results have shown that SHR after the lentiviral injection on the PVN, have lower levels of mean arterial blood pressure when compared to SHR group without the injection. This decrease in pressure is mainly due to a statistically significant decrease of the diastolic blood pressure which may be related to a decrease of the resistance of arterial vessels due to sympathetic activity. With these preliminary data we can speculate about the activation of PVN neurons in conditions of hypertension such that the silencing should reduce arterial pressure.

**Key-words:** Hypertension, Genetic modification (Kir2.1), Paraventricular Nucleus of the Hypothalamus