Abstract

The circadian system is an important coordinator of physiological functions of a mammalian organism. It comprises of a central oscillator represented by cells in the suprachiasmatic nuclei of hypothalamus (SCN) and peripheral oscillators in most if not all cells of peripheral tissues. The peripheral oscillators, similarly to the central ones, generate circadian oscillations at the level of so called clock genes and their protein products. In peripheral tissues, oscillations in expression of the individual clock genes are autonomous, however, they need to be synchronized to ensure their robust rhythmic expression. The peripheral clocks are synchronized mainly by rhythmical signals from the SCN, including signals regulating food intake. Disturbances in the clock gene expressions, as well as impaired synchronization signals, can result in various pathophysiological states. Spontaneously hypertensive rat (SHR) strain is a convenient animal model to study potential connection between the disturbed circadian system and progressive development of hypertension and metabolical diseases in mammals. Various studies have shown differences in the rhythmical expression of clock genes between SHR strain and normotensive Wistar/Wistar-Kyoto strain. The aim of this thesis is to provide insight into the early postnatal development of rhythmical expressions of clock genes Per1, Per2, Rev-erba and Bmal1 in the liver, distal colon and heart of SHR rats. The results show that the development of the rhythmical expression is tissuespecific. In vitro experiments performed on cultured fibroblasts demonstrate that the ability of SHR to respond to synchronization signals depends on developmental stage. Furthermore, in contrast to Wistar, SHR embryonic fibroblasts are not able to exhibit synchronous rhythmical expression of any of the clock genes after synchronization by glucocorticoids. Rhythmical expression of Per2, Rev-erba and Bmal1 mRNA is found in adult SHR fibroblasts, however, their levels are significantly lower when compared with fibroblasts from Wistar rats. The results of this thesis contribute to better understanding of differences of circadian systems in SHR and Wistar rats.

Key words: central clock, peripheral oscillators, clock genes, ontogenesis, synchronization, spontaneously hypertensive rat, fibroblasts, dexamethasone