

ABSTRACT

The circadian system temporally controls behavioral and physiological processes in most organisms so that they change during the day and night with a period of about 24 h. It is an evolutionary adaptation to anticipate periodic changes in environment on the Earth. In mammals, the circadian system consists of the central pacemaker in the suprachiasmatic nuclei (SCN) of hypothalamus and of oscillators located in numerous peripheral organs and tissues. At the molecular level, the circadian clock is based on the rhythmic expression of so called clock genes. The ontogenetic development of the circadian system is a gradual process and the most important changes undergo during the late embryonic and early postnatal stage. Many behavioral, hormonal and metabolic signals provided by the mother are considered to be involved in circadian clock synchronization during early ontogenesis. The mechanisms of the entrainment are not fully known yet. The aim of this thesis was to study the development of the circadian clock and its entrainment via maternal signals and to compare the development of circadian rhythms in two model rat strains – Wistar rat and spontaneously hypertensive rat (SHR).

Firstly, we described the ontogenetic maturation of the Wistar rat circadian clock in the colon from the fetal stage until weaning. Our findings suggest a molecular mechanism of how the colonic clock is entrained by maternal breast-feeding and propose a developmental switch from the maternal-dependent to maternal-independent stage. We found that an adult-like state was achieved around postnatal day 20.

Then, we compared the development of the circadian systems in Wistar rat and SHR and revealed significant differences in the dynamics of the SHR circadian system development and its sensitivity to changes in maternal-feeding regime. In the SCN and liver of SHR, the development of high-amplitude expression rhythm of canonical clock gene *Bmal1* was delayed. We also detected significant differences in maternal behavior between SHR and Wistar rats with a less frequent maternal care in SHR, which may be a factor contributing to the atypical development of the SHR circadian clocks during postnatal ontogenesis. To test this hypothesis, we performed cross-strain fostering set of experiments results of which revealed that the altered care provided by SHR mother worsened the entrainment of the central clock with the light/dark cycle in Wistar rat pups. The presumably better maternal care, provided by a Wistar rat mother to SHR pups, improved amplitude of the SCN-driven rhythms and their entrainment to external cues in adulthood. The peripheral clocks in the liver and colon responded more robustly to the cross-strain fostering and the response was not present in pups reared by a foster mother of the same rat strain.

Finally, we found out that in Wistar rat pups, combination of daily maternal stress with the mild arousal caused by pups manipulation increased their plasma-levels of glucocorticoids and shifted the rhythm of expression of clock gene *Bmal1* in the SCN. This effect was completely blocked by administration of the glucocorticoid receptor antagonist. In contrast, in SHR pups, maternal stress itself was able to shift the phase of the *Bmal1* expression rhythm in the SCN but this effect was probably not mediated via the glucocorticoid-dependent mechanism.