ABSTRACT

Glucocorticoids are mammalian steroid hormones secreted from the adrenal gland. The basal levels of glucocorticoids show a pronounced diurnal rhythm with maximum at the beginning of the active period and minimum at its end. Glucocorticoids have an influence over a variety of metabolic functions and their secretion is tightly regulated. This regulation also depends on the circadian system, which utilizes glucocorticoids to entrain the peripheral tissues by inducing rhythmic gene expression. The mechanisms by which glucocorticoids influence mammalian circadian system has not yet been precisely defined, especially concerning the influence of glucocorticoid signalling on gene expression in different tissues and the dynamics of glucocorticoid receptor (GR) occupancy. This thesis studies the influence of ablation of glucocorticoid signalization induced by adrenalectomy on the clock gene expression of in the central clock in the suprachiasmatic nucleus and peripheral clocks in the hippocampus and distal colon. The effect of adrenalectomy on gene expression is compared with the effect of restricting the feeding time, which has also been shown to affect glucocorticoid levels in the body. Other experiments were aimed at elucidating impact of changing the activity of GR on gene expression using synthetic GR antagonist in vitro. The results obtained by these experiments confirm the existence of peripheral clocks in the hippocampus including its individual parts and show the existence of tissue specificity of glucocorticoids on mammals.