Abstract

The main topic of this thesis are changes in Circadian rhythms caused by cerebellar disorders. Mice with Lurcher mutation, which have specifically degenerated Purkinje cells layer, were choosen as animal model. Our results show that mutation of the glutamate receptor GluRδ2, which causes gradual degeneration of Purkinje cells, leads to damage of Circadian system. Mice with this mutation have reduced capability to adapt to external conditions in different light modes. They are also showing increased variability in endogenous cycle. The mice are also unable to show anticipatory behavior in time-restricted feeding. Compared to control group, affected mice do not show significant rhythm in levels of protein of *Bmal1* gene in suprachiasmatic nuclei, paraventricular nuclei nor in habenula. Phosphorylated kinases ERK1/2 and GSK3ß also had distorted rhythms in suprachiasmatic nuclei. Because Circadian oscillations in locomotor activity are partly preserved, Circadian system is likely not damaged on molecular level. Cerebellar mutation hampers synchronization between suprachiasmatic nuclei of neurons and can also affect processes in the ventromedial hypothalamus regulating food intake.

Our findings are the first to suggest functional interactions between cerebellum and Circadian pacemaker in suprachiasmatic nuclei and likely also in habenula.