

Abstract

Huntington's disease (HD) belongs to neurodegenerative disorders. It is a monogenic disease caused by trinucleotide CAG expansion in exon 1 of gene coding protein huntingtin. Even though the cause of HD is known since 1993, the pathophysiology and cure for HD remains to be found. The animal models are being used for better understanding of HD. The most common animal models for HD are rodents, especially mice but it was also important to create large animal models, which will be more like human. Therefore, TgHD minipig was created in Academy of Science in Liběchov in 2009. This model was created by microinjection of lentiviral vector carrying N-terminal part of human HTT with 124 repetitive CAG in exon 1. This model is viable and in every generation, is part of the offspring transgenic.

In this thesis, I specialized to biochemical and behavioral changes of this model. I compared transgenic and wild type siblings. I found that biochemical changes are manifested mostly by increased level of mtHtt fragments in testes and brain. In behavioral part of this thesis I established new methods for testing behavioral changes in this model. The introduced methods showed some changes between wild type and transgenic animals at the tested ages but these changes were not significant due to the low number of animals at the oldest age. Nevertheless, these methods will be further used in aging animals to compare the phenotype development in this model with well-known behavioral and motoric changes typical for HD patients.

Keywords: Huntington's disease, huntingtin, animal model, miniature pig, behavioral studies