ABSTRACT

The memory and spatial navigation are extremely important brain functions for humans, but they are often the question of life and death for animals. In humans, memory can be disrupted by various neuropsychiatric disorders. The patients suffering from Alzheimer's dementia (AD) have impaired working and long-term memory, spatial navigation, higher cognitive functions and social memory. The deficit of cognitive coordination (the skill to recognize the relevancy of incoming information) and disorientation belong to the symptomatology of schizophrenia. Intelectual disability appears in some patients with autism spectrum disorder. Unfortunately, it is not possible to cure these disorders efficiently because the etiology is not known in the majority of patients. The causes leading to development of these disorders could be revealed using animal models. This thesis contributes to the characterization of the cognitive skills disruptions – as well as other behavioral alterations – in selected rat models of AD (transgenic McGill rat, non-transgenic Samaritan rat) and schizophrenia (lipopolysaccharide model of early postnatal, or prenatal, bacterial infection). The thesis also discusses the validity and limitations of these models. Our results showed a severe deficit of spatial navigation, learning and cognitive coordination in both AD models. In addition, the McGill rats manifested impaired motor coordination and balance problems, anxiety and changes in social behavior, reflecting the additional symptoms observed in human AD patients. The administration of lipopolysaccharide (LPS) in early postnatal life of rats did not lead to cognitive impairment in adulthood. However, it caused emotional disruption. We did not observe any other behavioral alterations in these rats. Validity of the postnatal LPS model is not fully clear because the emotional disruption is not specific and accompanies also other mental disorders. The rats after the maternal immune activation (prenatal LPS exposure) represent a valid model of schizophrenia, especially of the negative symptoms (we observed a higher startle reaction, prepulse inhibition deficit, reduced social interaction and changes in communication, anxiety, and hypoactivity). Nevertheless, the manifestation was dependent on sex and age of the animals, and the observed signs show some overlap with autism spectrum disorder as well. The cognitive impairment could not be measured in the LPS prenatal model as even the control rats were not able to acquire the task. Taken together, our findings demonstrate that the McGill rat is a useful model for the future AD research. The Samaritan rat requires more detailed examination. Moreover, it would be interesting to explore the ontogeny of the pathologies and mechanisms in the prenatal LPS rats.