## ABSTRACT

Methamphetamine (MA) is a synthetic psychostimulant that is one of the most abused drugs in the world. It is a member of the amphetamine group, and its popularity is based on its numerous rapid-onset stimulant effects, such as increased alertness, increased energy, decreased appetite, etc. However, in the long term, this drug has very serious consequences for the mental and physical health of individuals. Long-term use of MA causes severe impairment of central nervous system (CNS) function and associated behavioral changes. By virtue of its chemical similarity to monoamine neurotransmitters, MA interacts with their respective receptors and transporters. This phenomenon causes permanent damage to the terminal endings of neurons through the development of oxidative stress, neuroinflammation, and subsequently apoptosis. Thus, MA use causes various behavioral disorders, such as depression and psychosis and contributes to the outbreak of Alzheimer's and Parkinson's diseases. The use of such drugs can have a very serious impact during critical developmental periods, which are periods in which certain parts of the brain and the whole body are undergoing intensive development. Disrupting these processes can have irreversible consequences. These drugs are very often abused by pregnant women, who starve them for their stimulating effects. It has been observed that the use of MA by pregnant women has a negative impact on the development of the baby and its behavior. However, clinical studies are complicated because women who abuse this drug often abuse other drugs as well, and we do not know the concentration and purity of these substances, as well as how long they have abused this substance before and after pregnancy. Not only does MA cross the placenta, but it is also found in breast milk. However, the environment and upbringing of the individual are also important and can affect development positively or negatively. Animal studies are, therefore, useful. In our laboratory, it has been found that the negative effect on various cognitive functions in an adult exposed to MA prenatally depends on the stage of pregnancy at which the substance is administered. It has also been found that neonatal administration of this substance, specifically during the first 12 postnatal days, has a negative impact on the cognitive function of the individual. This period in the rat corresponds to the third trimester in man. Therefore, in this study, we decided to observe the effects of MA on adolescent subjects who were exposed to MA during the first 12 days of life. The animals were exposed to the drug both directly by subcutaneous injection and indirectly via breast milk when MA was given to the mothers. The animals were exposed to an enriched environment during development. After weaning, we performed several behavioral tests, which were mainly

used to test memory. Animals were grouped or separated after weaning. Separation is a stress factor that can also negatively affect the development of an individual. The results of behavioral tests showed us that separation has a greater negative impact on learning and memory than MA alone, but surprisingly, the enriched environment also had a negative impact in this case. In the next part of the experiment, we measured the levels of neurotransmitters, growth factors, as well as oxidative stress and c-fos at different stages of adolescence, namely in PD 28, PD 35 and PD 45. Neurotransmitter levels were also affected mainly by post-weaning stress, or the pre-weaning environment, as well as growth factors. Oxidative stress levels did not change depending on MA. C-fos expression was decreased during early and late adolescence following MA administration. Our results suggest that the administration of MA during the first 12 days has a less pronounced effect in the case of indirect administration and that the development and environment of the developing individual plays a critical role in this case.