Abstract

Aim: The aim of the Ph.D. thesis was to find out which of the neuro-ontogenetic stages of laboratory rat is more significant for the methamphetamine (MA) exposure on the behavior in adulthood and to determine a critical developmental period for the effects of this drug. In the experimental part of the study was to test the influence of prenatal and neonatal MA exposure on behavior, social interaction, cognition and drug-seeking behavior in adulthood.

Methods: Adult female rats were exposed to MA (5 mg/ml/kg) or saline (S) (1 mg/kg) during different stages of gestation and lactation. The tested substances were administered subcutaneously during the first half of gestation (ED 1-11), the second half of gestation (ED 12-22) or during early lactation (PD 1-11). The effect of prenatal MA exposure was transmitted to pups via placental barrier; the effect of MA exposure during early lactation was transmitted via the breast milk. In order to compare the rate of drug transmission by indirect MA exposure via the breast milk, we chose another group of offspring that we administered the tested substances directly subcutaneously during the same application period (PD 1-11). In this way we obtained 8 groups of exposed pups: ED 1-11 MA, S; ED 12-22 MA, S; PD 1-11 indirectly MA, S; PD 1-11 directly MA, S. These pups were tested in adulthood (PD 60-90) using behavioral tests for drug-seeking behavior (CPP), for social behavior (SIT), for behavior in unknown environment (Laboras test) and for learning and memory (MWM). To induce drug dependence in the CPP test, we exposed adult animals during the conditioning phase to MA in dose 5 mg/ml/kg. Our previous studies have shown increased susceptibility of offspring to acute MA after prenatal exposure to this drug, we applied acute dose of MA (1 mg/ml/kg) to half of animals in adulthood before/during the SIT, the Laboras and the MWM tests. The control group of animals was administered S (1 mg/kg). In adult female rats, phases of the estrous cycle were recognized and compared.

Results: The results of the study showed that prenatal and neonatal MA exposure did not affect drug addiction in adulthood, but induced deficits in social behavior, motor activity, and cognitive function of adult animals. Acute administration of MA (5 mg/ml/kg) in the CPP test created drug addiction in animals. Acute administration of MA (1 mg/ml/kg) decreased social behavior and increased

motor activity. In the MWM test, acute MA administration reduced the ability to remember the position of a hidden platform in animals exposed during ED 12-22. Adult female rats were more active in the SIT and in the Laboras test and achieved worse results in the learning and memory test. Females were more sensitive to acute MA during the proestrus/estrus. Direct exposure to MA subcutaneously during PD 1-11 led to more significant deficiencies in behavior than indirect exposure via the breast milk.

Conclusion: Based on our findings, we have concluded that the critical developmental periods for the effects of MA on behavior of animals in adulthood is the second half of prenatal development and early postnatal period in the laboratory rat, which corresponds approximately to the second and third trimesters of prenatal development in humans.