Neurobehavioral toxicity in Wistar rats offspring after prenatal exposure to different doses of diazepam

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Abstract

Neurobehavioral teratology is an important branch subject of neurobehavioral toxicology. It's methods are very sensitive and quantitative. Recently more and more researches are absorbed in the field of evaluating the safety of diazepam. To evaluate neurobehavioral teratological effect in rats offspring after prenatal exposure to diazepam with the methods of neurobehavioral teratology.

32 female and 16 male Wistar rats were mated on 3 months old. Diezepam were force-fed to pregnant rats during the 6^{th}~15^{th} day after conception with doses 0.00, 7.20,72.00, 360.00mg/kg/day. 21 pregnant rats were measured on physical development and reproductive process. The automatic operant behavior tests of 32 offspring were carried out at the age of 10 weeks. Moreover, the histological slides of brain in offspring were observed with light microscope, and the level of monamine neurotransmitter in brain was detected at the time of 10^{th} week of 24 offspring after delivery. Double blind was used in whole experiment.

Results of the experiment is that the maternal toxicity in rats after prenatal diazepam exposure was not observed in all treatment groups. Compared with the control group, some physiological and neurobehavioral development indexes of offspring in treatment groups were delayed, especially in high dose group ($P<0.05$ or $P<0.01$). There were also no significant differences in performance of operant behavior test in all treatment groups of offspring ($P>0.05$). No general histomorphological alterations in brains of offspring were observed in all groups. The level of monamine neurotransmitter in offspring's brains of all treatment groups was not changed compared with that of control group.

So this experiment finds that rat offspring exposed diazepam show some physiological and neurobehavioral development toxicity at the dose of not inducing maternal toxicity. Prenatal exposure to diazepam caused physiological development delay in all treatment groups and neurobehavioral development delay in high dose group, but abnormal function of memory and learning were not observed in rat offspring.

Through using the computer auto monitor system, the experiment involved the affect of surrounding environment and can make the results more sensitive and reliable. It is easy to find the early impairment of central nerve system combining many neurobehavioral teratology methods and quantity indexes. So the method will be widely used in public health, toxicology and pharmacology.

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Effect of combined pesticides during pregnancy on hippocampal _expression of NMDAR-1 protein in the offspring rats

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Abstract

Combined pesticides exposure during brain development is known to affect cognitive and be havioral functions in children and animals. The combined pesticides exposure on pregnant rat s from 1st to 15th day of gestation was used as a model to examine the _expression of NMDA R-1 protein in hippocampus DG CA1 CA3 area by immunohistochemistry (IHC) in the off-sp rings. The pregnant rats had been divided randomly into 4 groups. Three exposure groups wer e exposured to 1/300LD50, 1/95LD50, 1/30LD50 cypermethrion plus same equivalent does o f methylparathion respectively in vegetable sed oil since 1 day before mating. One control gro up were force-fed vehicle solvent only.Animals were deeply anaesthetized and perfused transc ardinally with 4% parafomaldehyde on 7days,14days,21days,28days after born. Cryostat secti ons of hippocampus were cut to 25 μm thickness. The rabbit anti-NMDA-R1 monoclonal anti body was used. The positive and negative controls were used in each test. After stained, a ligh t microscope was used to observe at regions of hippocampus DG CA1 CA3 area. In the contro l group, Level of NMDAR-1 protein _expression in hippocampus were lowest on 7th after bor n, increasing to reach peak levels by 21 days of age and subsequently decreasing at 28days of age. However, the peak of NMDAR-1 _expression in three does groups was at 8days of age.