Prenatal exposure to methamphetamine affects the development of the visual system of the rat

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The use of the drug methamphetamine (MA) has increased markedly in the last thirty years. It is known that this drug damage the developing central nervous system (CNS) and being the visual system part of the CNS, the retina and optic nerve are target tissues to MA exposure. Limited information is available regarding the effects of MA upon the developing visual system. The objective of the present work was to characterize the development of the rat visual system exposed during the prenatal period of development to MA. Pregnant females Wistar rats (n = 54) were exposed to a dose of MA (5 mg.Kg^{-1}/ day) from gestational day (GD) 8 to GD 22. The control group was pair-fed and saline injected. Morphometric analyses were performed at light and electron microscopic levels on optic nerve cross sections. Myelin basic protein (MBP) was measured by western blotting in optic nerve. For lipid peroxidation studies, retina were homogenized, and both the total antioxidant and superoxide dismutase (SOD) activities were measured by enzymatic-colorimetric methods. The lipid peroxidation by-products (malondialdehyde [MDA] and MDA-like metabolites) were measured by the thiobarbituric acid (TBA) test. Retinal monoamine (dopamine [DA] and 3,4-dihydroxyphenyl-acetic acid [DOPAC]) quantification was made by high performance liquid chromatography with electrochemical detection. The pattern of tyrosine hydroxylase (TH) immunoreactivity in the rat retina was also studied. Morphometric evaluations shown that the optic nerve mean cross-sectional area was reduced at PND14 in the male MA group, and in both the male and female groups at PND 21. Optic nerve diameter was reduced at PND 7 in the male MA group and in both male and female MA groups at PND 21. The total number of myelinated axons did not vary between groups at any of the studied ages. The myelin thickness of the axons in MA-treated females was thinner when compared with the respective control group at PND 21. There was a reduction of MBP protein expression in MA-injected females at PND 14 and PND 21. The total antioxidant levels were lower in the MA group at PND 21 both in males and females. The activity of SOD was higher in PND 7 females from the MA group. The MDA levels were higher in the MA female group at PND 21. Prenatal exposure to MA altered the levels of DOPAC in females at PND 30. No significant changes on the localization of TH immunoreactivity in the rat retina at PND 7, 14 and 30 could be detected between control and MA treated animals. Together, these results indicate that exposure to MA during critical periods of the CNS development affects the visual system structures that are forming. Moreover, the data presented in this study suggest a differential gender effect of MA, females being more susceptible to the neurotoxic effects of MA exposure.

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