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Attenuation by a novel synthetic analogue of ACTH₄₋₇ of the learning and memory deficits in juvenile rats treated with amphetamine *in utero*: role of nitric oxide

Valentina Bashkatova¹, Sergey Sudakov¹, Darya Rezvanova², Helmut Prast³ and Anatoly Vanin²

¹*Department of Neurochemical Physiology, P.K. Anokhin Research Institute of Normal Physiology RAMS, 125315 Moscow, Russia*

²*Department of Biophysics, Institute of Chemical Physics RAS, 119313 Moscow, Russia*

³*Department of Pharmacology and Toxicology, University of Innsbruck, 6020 Innsbruck, Austria*

E-mail: helmut.prast@uibk.ac.at

Background

Drug abuse among pregnant women continues at alarming frequency. Exposed children often show selective impairments of attention and other disturbances which might develop to major cognitive disorders. This work seeks to examine the impact of prenatal stress (PS) induced by the psychostimulant drug amphetamine (AMPH) on memory functions in male offspring of rats and to study the possible neuroprotective action of the novel Russian peptide Semax (a synthetic analogue of ACTH₄₋₇). In addition, the role of the neuronal messenger nitric oxide (NO) as well as the intensity of lipid peroxidation (LPO) in mechanisms of PS was examined.

Methods

Pregnant Wistar rats received a daily intraperitoneal injection of 10 mg/kg AMPH (IUAMPH) or saline for control dams (IUV) between E17 and E20. Nitric oxide generation was measured by electron paramagnetic resonance technique.

Results

Juvenile IUAMPH rats at 25 days of age showed delayed alternation deficits and impairments of acquisition of a fixed platform position in the water maze demonstrating impaired working memory. Both NO and LPO levels were elevated in the hippocampus of IUAMPH rats as compared with control animals. Pretreatment with Semax reversed the PS-induced learning deficits in offspring rats and prevented the increase of NO generation.

Conclusions

Thus, AMPH-elicited PS induces delayed memory deficits and significant learning impairments in juvenile offspring of rats. Therefore, *in utero* AMPH exposure resulted in a significant oxidative stress, which may be related to impaired learning ability. Modulation of the activity of NO and LPO might lead to a significant recovery of the memory functions in PS rats that open new approaches for neuroprotection and cognitive rehabilitation of prenatal brain damage.