Chronic neonatal MK-801 treatment in low doses decreases [^{3}H]MK-801 binding in striatum and impairs spatial acquisition in Morris water maze in the young rat

Latysheva NV[1,3], Pleskacheva MG[2], Saransaari P[3], Oja SS[3], Wolfer DP[4], Rayevsky KS[1]

[1] Research Institute of Pharmacology, RAMS, Moscow, Russian Federation
[2] Lomonosov State University, Moscow, Russian Federation
[3] Medical School, University of Tampere, Tampere, Finland
[4] Institute of Anatomy, University of Zürich, Zürich, Switzerland

N-Methyl-D-aspartate receptors (NMDAR) are known to play a crucial role in learning, memory and developmental neuroplasticity. It has been suggested that chronic blockade of this type of receptors in the early postnatal period results in spatial learning impairment which is probably associated with alterations of the NMDA receptor functional properties. In contrast to other studies (Gorter et al, 1992, *Brain Res*. 580: 12-17) we used nontoxic doses of noncompetitive antagonist of the NMDAR, dizocilpine (MK-801). Sprague-Dawley rat pups were daily treated with MK-801 in the doses of 0.05 mg/kg during the postnatal days (pd) of 7-11, 0.075 mg/kg pd12-16 and 0.1 mg/kg pd17-20. The possible alterations in the NMDAR-coupled ion channels were assessed by measuring [^{3}H]MK-801 binding to membrane preparations from the cerebral cortex, hippocampus, striatum, midbrain and cerebellum in 21-day-old animals. The binding was found to be diminished only in the striatum of the MK-treated rats. To examine the effects of chronic NMDAR blockade on the spatial learning and memory, Morris water maze testing (hidden platform) was performed in 30-day-old pups. MK-801-treated rats were able to learn the spatial task but significantly slower compared control rats while probe trial performance was not affected. Although the swimming speed was the same in both groups treated rats used ineffective learning strategy (thigmotaxis). In contrast with data of Gorter et al. our findings suggest that the cognitive deficit as a consequence of the chronic NMDAR blockade in the critical period of brain maturation was associated with an altered striatal function. An important role of striatum in the acquisition of spatial learning was shown by other authors (e.g. Devan et al, 1996, *Neurobiol Learn Mem*, 66: 305-23).