Effects of metabotropic glutamate receptor 5 antagonist MPEP on anxiety-like behavior in immature rats

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mGluR5 subtype of metabotropic glutamate receptors is present in various brain regions such as hippocampus, amygdala and cortex. An anxiolytic-like activity of the selective mGluR5 antagonist MPEP has been demonstrated in several conditioned and non-conditioned tests of anxiety in adult animals (for a review see [2]). In our laboratory, MPEP exhibited anticonvulsant actions in both adult and immature rats without inducing side effects on motor performance [3,4]. There are no studies dealing with effect of MPEP on behavior in developing animals. Therefore, we designed the present study to examine possible anxiolytic-like effect of the drug in immature rats particularly within the anticonvulsant dose range.

The experiments were performed in 18-, and 25-day-old Wistar rats. Experimental animals received i.p. 10, 20 or 40mg/kg of the drug, controls were injected with saline. Behavioral testing was performed 15 min (1^{st} session) and was repeated 60 min (2^{nd} session) following drug administration in the light-dark box [1]. The light-dark test is based on the tendency of animals to explore a novel environment vs. the tendency to avoid the aversive properties of a brightly lit arena. The individual rat was placed into the black part of the box facing the light part and its behavior was registered on a videotape for 5 min and scored using the Observer (Noldus Information Technology). The following parameters were evaluated: the time spent in light part, the number of transition between both parts and the number of squares crossed in the light part.

Compared with the controls, all doses of MPEP increased the time spent in the light part (a measure of anxiety-like behavior) in the 1st session in both 18- and 25-day-old rats, the

effect of 20 mg/kg dose being more expressed. All MPEP doses also increased the number of transitions between light and dark parts as well as the number of squares crossed in the light part in the 1^{st} session in either age group. There was a marked decrease in all measured behavioral parameters in the 2^{nd} session.

In conclusion, our data suggests that MPEP exerts anxiolyticlike activity also in immature rats without any sedation or suppression of locomotion. The decreased behavioral response in the 2nd session show that prior experience with the lightdark box may alter subsequent behavioral responsiveness of the immature animals to the light-dark test of anxiety.

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References

- Costall, B., Jones, B.J., Kelly, M.E., Naylor, R.J. and Tomkins, D.M. (1989). Exploration of mice in a black and white test box: validation as a model of anxiety, *Pharmacol Biochem Behav* 32, 777-85.
- Lea, P.M.t. and Faden, A.I. (2006). Metabotropic glutamate receptor subtype 5 antagonists MPEP and MTEP, *CNS Drug Rev* 12, 149-66.
- 3. Lojková, D. and Mareš, P. (2005). Anticonvulsant action of an antagonist of metabotropic glutamate receptors mGluR5 MPEP in immature rats, *Neuropharmacology* **49**, Suppl 1, 219-29.
- Mareš, P. and Mikulecká, A. (2004). MPEP, an antagonist of metabotropic glutamate receptors, exhibits anticonvulsant action in immature rats without a serious impairment of motor performance, *Epilepsy Res* 60, 17-26.