

# 8<sup>th</sup> European Neurology Congress

September 21-23, 2016 Amsterdam, Netherlands

## Neuroprotective effects of metabotropic glutamate receptors group II (mGluR2/3) agonists in an animal model of birth asphyxia

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**Introduction:** Hypoxic-ischemic encephalopathy (HIE) results in permanent damage of central nervous system that may result in neonatal death or developmental disorders. 20%–30% of infants with HIE die in the neonatal period and 33%–50% of survivors demonstrate permanent neurodevelopmental abnormalities (such as cerebral palsy) and mental retardation. It was shown recently that group II metabotropic glutamate receptors (mGluR2/3) activation before or after ischemic insult results in neuroprotection but the exact mechanism of this effect is not clear.

**Aim of the study:** The aim of present study was to investigate whether mGluR2/3 activation after experimental hypoxia-ischemia reduces brain damage and if the reduction of the expression of pro-apoptotic factors is one of the mechanisms involved.

**Methods:** We used an animal model of hypoxia-ischemia (H-I) on 7-day old rat pups. Animals were anesthetized and the left common carotid artery was isolated, double-ligated and then cut between the ligatures. After completion of the surgical procedure the pups were subjected to hypoxia (7.4% oxygen in nitrogen for 75 min at 35 °C). Control pups were sham-operated (anaesthetized and left c.c.a. dissected, but not ligated). Animals were injected intra-peritoneal with specific mGluR2 (LY 379268) and mGluR3 (NAAG) agonists 24 h or 1 h before H-I (5 mg/kg of body weight). The weight deficit of the ischemic brain hemisphere was measured and the expression of Bax, Bcl-2 and HTR/OMI was examined. The damage in the hippocampal CA1 region was examined by Cresyl violet (CV) staining. Also the differences in the expression of neurotrophic factors (BDNF, GDNF, TGF-β) were measured (ELISA).

**Results & Discussions:** Our results show that application of mGluR2/3 agonists before H-I results in neuroprotection. Application of both agonists resulted in decrease in brain tissue weight loss in ischemic hemisphere independently on the time of application (from 40% in H-I to 15 - 20% in treated). Histological examination of the brain tissue showed that both mGluR2/3 agonists applied 24 h or 1 h before H-I decrease the damage of neuronal cells and the disorganization of CA1 region of hippocampus. In our study we also observed the relative changes in the expression of Bax, Bcl-2 and HTR/OMI proteins in ipsilateral and contra-lateral hemisphere. Both agonist mGluR2/3 applied 24h or 1h before H-I decreased expression of Bax and HTR/OMI and increased expression of Bcl-2 in the ischemic brain hemisphere compared to untreated H-I. Both mGluR2/3 agonists (LY379268 and NAAG applied 24h or 1h before HI) decreased TGF beta expression and increased BDNF and GDNF expression in the ischemic brain hemisphere compared to H-I.

**Conclusions:** Our results show that activation of mGluR2 or mGluR3 in a short time before H-I insult reduce brain damage in 7-day old rats and decrease apoptotic processes initiated by HI in developing brain. These results suggest that activation of group II mGluR before H-I triggers mechanisms that result in neuroprotection.

### Biography

Ewelina Bratek is PhD student in Dept. of Neurochem at Mossakowski Medical Research Centre, Polish Academy of Sciences, Warsaw, Poland. Ewelina Bratek has published more than 3 papers in reputed journals.

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