Neuroprotective effects of MTEP, a selective mGluR5 antagonist and neuropeptide Y on the kainate-induced toxicity in primary neuronal cultures

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Abstract:
The majority of studies on neuroprotection tested potentially protective compounds given before, simultaneously or shortly after damage. Such procedures are greatly different from the situation faced in clinical practice. In the present study, we tried to find out whether two compounds, a selective mGluR5 antagonist 3-[(2-methyl-1, 3-thiazol-4-yl) ethynyl]-pyridine (MTEP) and neuropeptide Y (NPY) elicit neuroprotective action against excitotoxic damage in the mouse neocortical and hippocampal neuronal cultures after delayed treatment. In order to evoke toxic effects, primary cultures were exposed to 150 µM kainic acid (KA) for 24 h (hippocampus) or for 48 h (neocortex). MTEP (1, 10 and 100 µM), or NPY (0.5 µM and 1 µM) were applied 30 min before, or 30 min, 1 h, 3 h or 6 h after KA. Kainate neurotoxicity was measured by lactate dehydrogenase (LDH) efflux from the damaged cells into the culture media. The results of our studies showed that MTEP or NPY treatment attenuated the kainate-induced LDH release in mouse neocortical and hippocampal cultures. The effect was observed when the compounds were added not only before, but also 30 min to 6 h after KA. Moreover, both MTEP and NPY displayed antiapoptotic activity as they prevented the KA-induced increase in the expression of caspase-3 activity in the cultures under study. Summing up, our data showed that MTEP and NPY were neuroprotective in wide time schedule. The effectiveness of late treatment with these compounds opens a new perspective for their potential therapeutic use.

Key words: neuroprotection, mGluRs, MTEP, NPY, kainic acid, excitotoxicity, primary neuronal cultures