Abstract:

Cortical glial cells contain both ionotropic and metabotropic glutamate receptors. Despite several efforts, a comprehensive analysis of the entire family of glutamate receptors and their subunits present in glial cells is still missing. Here, we provide an overall picture of the gene expression of ionotropic (AMPA, kainate, NMDA) and the main metabotropic glutamate receptors in cortical glial cells isolated from GFAP/EGFP mice during ageing as well as before and after focal cerebral ischemia. Employing single-cell RT-qPCR, we detected the expression of genes encoding subunits of glutamate receptors in cortical GFAP/EGFP-positive (GFAP/EGFP$^+$) glial cells. Most of the analyzed cells expressed mRNA for glutamate receptor subunits, the expression of which, in most cases, even increased after ischemic injury. Data analyses disclosed several classes of GFAP/EGFP$^+$ glial cells with respect to glutamate receptors and revealed in what manner their expression correlates with the expression of glial markers prior to and after ischemia. Furthermore, we also examined the protein expression and functional significance of NMDA receptors in glial cells. Immunohistochemical analyses of all seven NMDA receptor subunits provided direct evidence that the GluN3A subunit is present in GFAP/EGFP$^+$ glial cells and that its expression is increased after ischemia. In situ and in vitro Ca^{2+} imaging revealed that Ca^{2+} elevations evoked by the application of NMDA were diminished in GFAP/EGFP$^+$ glial cells following ischemia. Our work provides a comprehensive description of glutamate receptors in cortical GFAP/EGFP$^+$ glial cells and may serve as a basis for further research on glial cell physiology and pathophysiology.

Keywords: astrocytes, NG2 glia, glutamate receptors, NMDA receptors, MCAO