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# The concentration-dependent neo- and allocortical effect of GYKI 52466 in the 4-aminopyridine-induced acute rat seizure model

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The activation of ionotropic glutamate receptors leads to the expression of transcription factor c-fos via protein-phosphorylation cascades. In former studies we have proved that the antagonists of N-methyl-D-aspartate (NMDA)-receptor significantly reduce the c-fos gene expression in 4-aminopyridine (4-AP)-induced acute convulsions in the rat cerebral cortex. In the present study we have examined the supposed relation between the activation of α-amino-3-hydroxy-5-methyl-4-izoxazol-propionate (AMPA)-receptors and c-fos expression in 4-AP-induced convulsions. According to our previous data, the seizure activity is accompanied by oedematous changes in the astrocytic endfeet around the cerebral capillaries.

As an antagonist of the AMPA-receptor, GYKI 52466 has been administered in 25 and 50 mg pro bwkg doses, intraperitoneally. The control groups received the solvent of this antagonist. Then, acute convulsion was elicited by the intraperitoneal administration of 4-AP (in 5 mg/kg dose) in pretreated and control groups, as well. The latency of the well-defined seizure symptoms was measured. After one hour observation time, the animals were sacrificed, the brains processed either for double-labelling light microscopic immunohistochemistry, (for c-fos and parvalbumin (PV) detection) or for electronmicroscopy (capillary lumen area and surrounding oedematous changes); focusing on the parietal neocortex and on the hippocampus. The number of immunoreactive cell nuclei pro area unit ($mm^2$) was quantified and the capillary and pericapillary areas were measured, then statistical analysis was performed on the gained data.

In the AMPA-antagonist pretreated groups the latency of generalised tonic-clonic seizure (GTCS) was prolonged, no recurrent seizure was observed; the survival of the animals was 100%. In the neocortex, the higher antagonist dose caused a significant decrease in c-fos expression, mainly in the neocortical II-III and V-VI laminae. This effect was present in case of c-fos + PV double-labelled cells in a dose-dependent fashion. In the examined allocortical areas even the lower dose antagonist pretreatment moderated significantly the c-fos positive and c-fos+ PV double-labelled cell count. The lower dose pretreatment seems to be aggravate the oedematous changes, whereas the effect of the higher dose pretreatment statistically is not contributive. The reduction of this activity-dependent neuronal marker was more remarkable in the allocortical than in the neocortical areas, pointing to the difference in the AMPA-receptor distribution. To decrease the c-fos expression in PV-positive cells, a lower antagonist dose was sufficient enough, showing the significance of the AMPAergic input of this cell subpopulation. According to the statistical data, the AMPAergic mediation may not be the primary component influencing the oedematous changes of the pericapillary areas in the rat brain.

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