P4.25.

Changes in the distribution of the ClC-2 Cl- channel in the chronic phase of epilepsy

Karlócai, R.[1]; Maljevic, S.[2]; Tóth, K.[1]; Csizmadia, T.[1]; Freund, T. F.[1]; Lerche, H.[2]; Maglóczky, Z.[1]

1: Institute of Experimental Medicine, Hungarian Academy of Sciences
2: Dept. of Neurology and Epileptology, Hertie Institute for Clinical Brain Research, University Hospital Tübingen, Germany

Impairment of GABAergic inhibition is known to be a possible cause of epileptic activity. Since the transmembrane Cl- gradient determines the direction and magnitude of current mediated by GABAA receptors, its alterations are of crucial importance in understanding epileptogenic mechanisms. Chloride homeostasis is regulated by transporters and chloride channels. ClC-2 constitutes an exclusive chloride extrusion pathway, since it only opens at potentials more negative than the Cl- equilibrium potential. We developed a new antibody against ClC-2, and examined the distribution of ClC-2 in the hippocampi of control and knock-out mice. Glial elements (endfeet) surrounding the blood vessels proved to be positive, mainly in stratum moleculare and stratum lacunosum-moleculare. Outside the hippocampus the strongest staining appeared in layer V. pyramidal cells of the neocortex, as described earlier. This staining pattern was absent in ClC-2 KO mice. Epilepsy was induced by pilocarpine, after one month of survival the distribution of ClC-2 was examined. In the epileptic mice with sclerosis, the localization of ClC-2 was changed. Beside the endfeet, the somata and processes of glial cells were stained in the hilus, and in the stratum moleculare of the DG. Astroglial cells are involved in delivering and redistributing chloride. Due to seizure activity, ionic fluxes may require more effective Cl- siphoning mechanisms to cope with the altered Cl- homeostasis.

Support: EPICURE LSH-CT-2006-037315