LAMINAR AND SUBCELLULAR HETEROGENEITY OF GLAST AND GLT IMMUNOREACTIVITY IN THE DEVELOPING POSTNATAL MOUSE HIPPOCAMPUS

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Astrocytes express two sodium-coupled transporters, GLAST and GLT-1, which are essential for the maintenance of low extracellular glutamate levels. Here, we performed a comparative analysis of the laminar and subcellular expression profile of GLAST and GLT-1 in the developing postnatal mouse hippocampus using immunohistochemistry and western blotting and employing high-resolution fluorescence microscopy. Astrocytes were identified by costaining with GFAP or S100s. In CA1, the density of GFAP-positive cells and GFAP expression rose during the first two weeks after birth, paralleled by a steady increase in GLAST immunoreactivity. Up-regulation of GLT-1 was completed only at postnatal days (P) P20-25 and thus delayed by about ten days. Western blots further revealed a differential upregulation of multimeric and monomeric forms of GLAST and GLT-1 during this period. GLAST staining was highest along stratum pyramidale and was preferentially expressed in astrocytes at P3-5. GLAST immunoreactivity showed no preferential localization to a specific cellular compartment. GLT-1 exhibited a laminar expression pattern from P10-15 on, with highest immunoreactivity in the stratum lacunosum-moleculare. At the cellular level, we found that GLT-1 immunoreactivity did not entirely cover astrocyte somata and exhibited clusters at perisynaptic processes. In juvenile animals, discrete clusters of GLT-1 were also detected at perivascular endfeet. Our results thus uncover a hitherto unnoticed and remarkable subcellular heterogeneity of GLAST and GLT-1 expression in the developing hippocampus. The clustering of GLT-1 at astrocyte endfeet indicates that it might serve a specialized functional role at the blood-brain barrier during formation of the hippocampal network.