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ANATOMICAL ANALYSIS OF TYPE-I CANNABINOID RECEPTORS IN HIPPOCAMPAL ASTROCYTES OF MUTANT MICE

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Type-1 cannabinoid (CB1) receptor is widely expressed in the brain mediating the effects of (endo)cannabinoids. Evidences have shown its activation in astrocytes might be playing an important role in neuronal modulation of synaptic transmission and plasticity. To identify low levels of CB1, avoiding their misinterpretation as background staining; “rescue” strategies are needed. However, it is necessary to evaluate if genetic re-expression maintains normal CB1 expression in specific cell types of the “rescue” mutants. We analyzed the subcellular CB1 distribution in astrocytes of the dentate molecular layer. We used conditional “CB1 rescue mice” which re-express CB1 only in astrocytes (GFAP-CB1-RS mice) and transgenic mice carrying GFP under the control of the GFAP promoter (GFAP-GFP mice). Specific CB1, GFAP and GFP antibodies combined with a preembedding immunogold and an immunoperoxidase method for electron microscopy were applied to hippocampal sections of the mutants, as well as of CB1-WT and of CB1-KO mice that were used as controls. The results showed that 40.69% ± 3.69% of astrocytic sections were CB1 immunopositive in GFAP-CB1-RS. No significant differences were observed comparing with CB1-WT (44.81% ± 3.62%). Sparse unspecific particles were detected in a few astrocytic elements of CB1-KO (1.77% ± 0.72%) and GFAP-CB1-KO mice (3.08% ± 1.03%). In GFAP-GFP mice, 51.68% ± 2.70% of the GFP immunoreactive astrocytic processes were CB1 positive (significant difference compared to CB1-WT, *; p< 0.05). To summarize, the proportion of CB1 immunopositive astrocytic processes in CB1-WT is maintained in GFAP-CB1-RS mice, showing the great potential of these transgenic mice to study CB1 in brain cell types where the CB1 expression is low. Besides, more CB1 positive astrocytic processes were observed in GFAP-GFP mice, suggesting that a better CB1 detection in astrocytes can be achieved in these reporter mice. The expression of CB1 in astrocytes might be higher than what was expected.