Kar-mediated glutamate release facilitation at mossy fiber-ca3 synapses of the hippocampus involves calcium-calmodulin and a high calcium threshold

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Kainate-type glutamate receptors (KAR) participate in conventional neuronal transmission and processes like Long-Term Potentiation (LTP) and Long-Term Depression (LTD) that are believed to be responsible of the plastic changes that occur in the CNS during development, learning and memory and recovery after CNS lesions. The inadequate activation of KARs has detrimental effects that have been related to excitotoxicity, epilepsy and other disorders. The hippocampus is a sensitive region for epilepsy and KARs have been suggested as mediators of some of the epileptic effects of the potent neurotoxine kainate. At mossy-fiber hippocampal synapses presynaptic activation of KARs modulates glutamate release but the mechanisms involved in this modulation are not entirely known. The aim of this work was to establish the mechanisms involved in glutamate release facilitation mediated by KAR-activation at mossy fiber-CA3 synapses in mice. We used whole-cell patch-clamp recordings for this purpose. We found that activation of presynaptic KARs facilitated glutamate release via activation of adenylate cyclase (AC) by the Ca^{2+}- calmodulin complex. This effect was highly-dependent on the intracellular Ca^{2+} levels and involves the entry of Ca^{2+} by L- type voltage-gated calcium channels, GluK1 containing KARs, and Ca^{2+}-induced Ca^{2+} release from intracellular stores. Nest step of our research is to determine whether preventing the activation of this cascade prevents some of the epileptogenic effects of kainite.