IMPACT OF MATRIX METALLOPROTEINASES ON LONG-TERM GABAERGIC SYNAPTIC PLASTICITY IN THE SCH-CA1 HIPPOCAMPAL PROJECTION

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Matrix metalloproteinases (MMPs) play an important role in excitatory synaptic transmission, learning and memory. Recently, we have shown that MMP-9 is involved in LTP induced by the spike timing-dependent plasticity paradigm in the barrel cortex of mouse (Lebida and Mozrzymas, 2016) and that MMP-3 activity supports plasticity via regulation of NMDARs function in stratum radiatum of CA1 hippocampal region (Brzdak et al., 2017). Besides glutamatergic synapses also inhibitory synapses exhibit several forms of long-term plasticity. However, contribution of MMPs on long-term GABAergic synaptic plasticity have not been investigated so far. To address this issue, we have considered both inhibitory long term potentiation (iLTP) and depression (iLTD) in acute hippocampal slices (P18-P21). We made an attempt to induce iLTP either by transient exposure to NMDA (3 min, 20μM) or by reverse spike timing protocol whereas iLTD was induced by forward pairing (in the presence of DNQX, Vh = -40 mV). We found that following NMDA treatment a stable increase in GABAergic mIPSCs took place indicating successful iLTP induction (mIPSC amplitudes potentiation 22±8%, n = 7). In the case of the reverse pairing, a stable iLTP was observed only in a fraction of recordings while in remaining experiments an opposite or no effect were observed. This variability was probably due to recruitment of different sets of interneurons innervating pyramidal cells from which recordings were made. We found that in the presence of bath applied metalloptroteinases inhibitor, FN-439 (180μm), transient NMDA application initially induced an increase in mIPSC amplitudes but this effect was not stable and mIPSC amplitudes returned within up to ten minutes to the baseline level (in FN-439: 98±6%, n = 7 at 22-24 min after NMDA application $p<0.05$ in comparison to control). On the contrary, iLTD induced by reverse pairing was resistant to MMPs inhibitor (CTR 70±6%, n = 15, FN-439 67±5%, n = 13 $p>0.05$). Thus in Sch-CA1 hippocampal projection i-LTD does not depend on the activity of MMPs. In conclusion, we provide the first evidence for involvement of extracellular proteolysis in the GABAergic plasticity.

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