Abstract Information

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Title :	5-HT4 receptors of the medial Prefrontal Cortex impair the induction of a long-term potentiation within the Dentate Gyrus
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Abstract :

In order to determine to what extent the rapid antidepressant (AD)-like effects related to (i) increased synaptic plasticity or (ii) the administration of 5-HT4 agonists share common mechanisms, we aimed at investigating the role of 5-HT4 receptors (5-HT4-R) in the modulation of synaptic plasticity within the dentate gyrus (DG). The first step was to dissociate the global influence of 5-HT4 agonists from their direct effects on DG neurons. Indeed, these compounds are known to increase central 5-HT activity through a long-loop feedback originating within the medial prefrontal cortex (mPFC). To this end, we used small hairpin RNAs (shRNA) expressed by lentiviruses (LV) to inhibit the expression of 5-HT4 receptors specifically in the mPFC. Then, we assessed the effect of the 5-HT4-R selective agonist prucalopride on the long-term potentiation (LTP) induced within the DG of anesthetized rats by high frequency stimulation (HFS) of its main afference, the perforant pathway. In animals non injected with LV, an acute treatment with prucalopride (5 mg/kg, i.p.) reduced the success rate of LTP comparatively to the vehicle (field potentials: 54 vs 82%, population spike: 55 vs 100%), without any significant effect on LTP amplitude. The continuous treatment for 3 days with prucalopride (5 mg/kg, s.c.) further reduced the success rate of LTP to 27% for the field potentials, without changing its amplitude. For spike population, the success rate of LTP was the same as in acute conditions, but with a significant decrease of its amplitude. In LV-treated rats, acute prucalopride induced a successful LTP in 91% and 86 % of the cases for field potentials and spike population, respectively (no change in LTP amplitudes). Experiments addressing the effects of a 3-day treatment in LV-injected animals are currently underway.

Together, our results support an important role for 5-HT4-R in the modulation of hippocampal synaptic plasticity. It appears that 5-HT4-R located in the mPFC hinder the induction of LTP, which is restored to normal levels after their knockdown.