Distinct regulation of morphine-induced conditioned place preference and withdrawal in MDGA1 knockout mice

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MAM domain glycosylphosphatidylinositol anchor 1 (MDGA1) is one of the extracellular anchor proteins which belong to immunoglobulin superfamily. MDGA1 negatively regulates inhibitory synapse via selective interaction with Neuroligin-2. Neuroligin-2 is expressed in inhibitory GABAergic neurons, and contacts synaptic terminals to form synapses including dopaminergic synapses which play a key role in rewarding systems. We previously reported that MDGA1 knockout mice actually show enhancement of inhibitory perisomatic synaptogenesis in hippocampus and impairment of cognitive functions. In this study, we investigated the characteristics of morphine-induced dependence in MDGA1 knockout mice. Acquisition of morphine-induced conditioned place preference (CPP) in MDGA1 knockout mice was slightly increased while extinction of morphine CPP was strongly impaired. In contrast, naloxone-precipitated morphine withdrawal signs were decreased in MDGA1 knockout mice. These results demonstrate that MDGA1 can help the extinction of morphine-induced reward but make the expression of somatic withdrawal signs worse.