Dlx-5/6Cre-mediated conditional gene knockout of the delta opioid receptor: implications on behaviour

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Delta opioid receptors are G-protein coupled receptors belonging to the opioid system, which plays a central role in pain control, hedonic homeostasis, mood and well-being. These receptors are strongly expressed in olfactive bulb, cortex, striatum, basolateral nucleus of the amygdala and pons nuclei. Using constitutive gene knockout, we have previously shown a role for delta receptors in anxiety-related behaviors [1] as well as in chronic pain [2] and impulsivity [3]. In order to further investigate circuit mechanisms of delta receptor-mediated in anxiety-related and depressive-like behaviours, we developed a conditional knockout mice line (cKO), to produce a specific deletion of DOR in GABAergic neurons of the forebrain. We bred mice with a floxed delta receptor gene (*Oprdm1* fl/fl) with a driver transgenic Dlx-5/6-Cre line [4]. We first determined the brain distribution of delta receptors in cKO F2 offspring (Dlx5/6-Cre Tg+ X *Oprdm1* fl/fl) at mRNA level by RT-qPCR and protein level by quantitative autoradiography and [35S]GTPγS binding experiments. We observed dramatic reduction of receptor expression in the olfactive bulb and striatum of cKO mice, both at mRNA and protein levels. In both cortex and hippocampus receptor deletion was partial, and no change was detected in the amygdala, pons nuclei and the spinal cord. We initiated behavioural characterization of the cKO line in comparison with control littermates and constitutive knockout mice. Animals were tested in the light/dark box, the elevated plus maze and the open field tests for anxiety behaviours and in the forced swim and tail suspension paradigms for depressive-like behaviors. Our data show that, as previously described, constitutive knockout mice exhibit higher level of anxiety-related and depressive-like behaviours, however no significant difference was observed between cKO mice and their controls in these tasks. Our current study addresses behavioural responses known to recruit striatal, hippocampal and cortical circuits.

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