CB1 Receptor Modulates Social Investigation in Mice

Ana Luisa Terzian[1,2], Vincenzo Micale[3], Carsten T. Wotjak[0]. [1]Max-Planck Institute of Psychiatry, Munich, Germany, [2]Graduate School of Systemic Neuroscience / LMU, Munich, Germany, [3]CEITEC (Central European Institute of Technology) Masaryk University, Brno, Czech Republic

Introduction Social abnormalities can be found in almost all psychiatric disorders – such as anxiety, depression and schizophrenia. Thus, comprehension of the neurobiological basis of social interaction is an important feature to better understand several pathologies and improve possible treatments. Several evidences suggest that an alteration of cannabinoid CB1 receptor (CB1R) function could be involved in the pathophysiology of such psychiatric disorders. However, the role of CB1R still unclear and its localization on different neuronal subpopulations may produce distinct outcomes.

Aim The aim of the present study was to dissect the role of CB1R on different neuronal population, particularly on GABAergic and Glutamatergic neurons, in social behavior.

Methods Male knockout mice and their control littermate (C57BL/6 background) [conventional (ubiquitous deletion of CB1R – $CB1^{-/-}$) or conditional (specific deletion of CB1R on cortical glutamatergic neurons ($GluCB1^{-/-}$) or in GABAergic interneurons ($GabaCB1^{-/-}$)], and wild-type (WT) mice treated with CB1R antagonist/inverse agonist SR141716A or vehicle (3mg/kg; i.p. dissolved in 2.5%DMSO in saline) were submitted to the social investigation task. In this test, mice were habituated for 10min to a 3-chamber-box (30 cm × 30 cm × 30 cm) with two empty falcon tubes on each side. Next, one of the tubes was replaced with another falcon tube containing a male or an ovariectomized female mouse. The animals were allowed additional10min of exploration.

Results $CB1^{-/-}$ presented less interest for social investigation towards a female stimulus compared to control (n= 13-16; time: $F_{1,27} = 7.17$, $p<0.005$; episodes: $F_{1,27} =10.16$, $p<0.005$). This difference was less evident when a male stimulus was used (n=6-7). WT mice treated with CB1R SR141716A also presented reduced social interest for female (n=6-7; time: $F_{1,12}=5,99$, $p<0.05$; episode: $F_{1,12}=10.03$, $p<0.05$), and also, male subjects (n=9-10; time: $F_{1,17}= 26.97$, $p<0.05$). $GluCB1^{-/-}$ exhibited little interests for the female (n=8-10; time: $F_{1,16}=4.65$; $p<0.05$; episode: $F_{1,16}=5.97$; $p<0.05$), while showing similar levels of investigation as control group upon a male (n=10). $GabaCB1^{-/-}$ demonstrated the opposite behavior as $GluCB1^{-/-}$ mice when exposed to females (n=11; time: $F_{1,21}=18.35$, $p<0.001$; episode: $F_{1,21}=14.16$, $p<0.05$), i.e. they showed increased interest; however, when exposed to male subjects, they showed no difference compared to control group (n=7-10).

Conclusion CB1 receptors modulate social behavior in mice, and the motivational aspect of the social stimulus is of relevance. CB1R exhibits different responses in a cell-specific manner – CB1R on glutamatergic neurons promotes whereas CB1R on GABAergic neurons reduces social investigation of a female mice. Therefore, CB1 receptor is a target of interest in the study of psychiatry disorders.