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Endocannabinoidome genetic impact in the neurobiology of drug addiction and autism spectrum disorders.

The discovery of additional lipid mediators, enzymes, receptors, paracannabinoids, has broadened the endocannabinoid system (ECS) into what is now termed the endocannabinoidome (eCBome). Cannabis has been used as medicine for millennia and we are just beginning to uncover its medical potential as research suggests that more promising breakthroughs are yet to come. With recent attempts at cannabis marijuana reclassification will enhance eCBome research as therapeutic targets. eCBome probing may enhance and unravel novel avenues in neurobiological disorder targeting genetic and neuroimmune profiles and recognizing salience in neural pathways. Autism spectrum disorders (ASDs) are neurodevelopmental disorders, which are uniquely human, and some of the characteristics can be mimicked by BTBR T+tf/J mice. Neuroinflammation is emerging as a key component of many disorders including drug addiction and ASDs. We have used Cnr2 conditional knockout (cKO) mice with deletion of CB2Rs from microglia (CX3Cr1-Cnr2) and dopamine (DA) neurons (DAT-Cnr2) respectively. In a separate study we used BTBR T+tf/J mice model of ASDs. The aim is to gain deeper insights into genetics of eCBome impact in the neurobiology of drug addiction and autism spectrum disorders. We found that the BTBR mice exhibited enhance spontaneous activity and a reduced depressogenic profile with a cannabinoid CB2A gene expression upregulated. However biased cell-type CB2R signaling pathways were observed in dopaminergic and microglia specific CB2R deletions. The studies show CB2R modulatory effects on neuroinflammation and may be potential therapeutic target in drug addiction and CNS disorders associated with neuroinflammations like ASDs.

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