Cannabinoid 2 receptor inhibition reverses immunosuppression following acute CNS injury in mice

Ian Burkovskiy¹, Juan Zhou¹, Christian Lehmann¹
¹Dalhousie University

Acute CNS injury leads to disturbance of the normally well-balanced interplay between the immune system and the CNS. This dysregulation has been termed CNS injury-induced immunodeficiency syndrome (CIDS). The endocannabinoid system (ECS) plays a role in homeostatic regulation of the immune system. Cannabinoid 2 receptor (CB2R) activity is associated with immunosuppression. We investigated if CIDS can be reversed by inhibiting CB2R activity using the CB2R antagonist, AM630.

CNS injury was induced in C57Bl/6 mice via an intracerebral injection of endothelin-1. The immune system was challenged with endotoxin 24 hours later. Intravital microscopy was used to study the peripheral immune response within the intestinal microvasculature. Brain tissue was stained with triphenyl tetrazolium chloride to measure the infarct size. In addition to CB2R inhibition, the effect of genetic CB2R knockout on the severity of CNS injury, as well as the severity of CIDS was investigated.

Results showed that animals with CNS injury have a reduced immune response to endotoxin when compared to animals without CNS injury. AM630 administration 15 min prior to LPS challenge, reversed this measure of suppressed immune function and did not have any detrimental impact on the infarct size. Genetic knockout of CB2R revealed that the CIDS was not induced after an acute CNS injury, confirming the involvement of the ECS in CIDS. Further studies should investigate the optimal treatment window for CB2R therapy.