ROLE OF CANNABINOID 2 RECEPTOR ACTIVITY IN POST CNS INJURY IMMUNODEFICIENCY

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BACKGROUND

RESULTS

- ❖ Patients after acute central nervous system (CNS) injury have a high risk for an infection due to post-injury disturbance of the normally well-balanced interplay between the immune system and the CNS resulting in systemic immunosuppression, as shown in Figure 1 below.
- ❖ The endocannabinoid system (ECS) is composed of endocannabinoids, specific receptors and metabolizing enzymes, and is involved in key homeostatic functions in the CNS and the immune system
- ❖ The cannabinoid 2 receptor (CB2R) on immune cells and microglia presents a potential therapeutic target as activation of this receptor has been shown to be involved in immunosuppression.
- ❖ Our study presents experimental evidence that targeting the CB2R may have beneficial effects on the outcome after an acute CNS injury
- ❖ The **main objective** of the study was to investigate if post CNS injury immunodeficiency can be reversed by - (1) early activation of CB2R using a synthetic agonist HU308 (2.5 mg/kg, i.v.); (2) late deactivation of CB2R using a synthetic CB2R antagonist AM630 (2.5 mg/kg, i.v.)

Figure 2. (A) Leukocyte adhesion in collecting venules (V1); *p<0.05 vs CON, ** p<0.05 vs LPS, # p<0.05 vs CNS INJURY+LPS (B) Infarct volume, as measured after TTC stain *p<0.05 vs CNS INJURY

Figure 3. (A) Leukocyte adhesion in collecting venules (V1) in CB2R K.O. mice; *p<0.05 vs CON, (B) Infarct volume in CB2R K.O. mice, as measured after TTC stain *p<0.05 vs WT

MATERIALS & METHODS

CONCLUSION

- ❖ **Species:** Male C57BL/6 w.t. and CB2R K.O. mice (6-8 weeks). All drugs were administered intravenously.
- ❖ **CNS Injury Model:** CNS injury was induced via two intracerebral injections of a vasoconstrictor peptide, endothelin-1 (ET-1, 2µg/µl) into mouse cortex.
- ❖ **Microscopy:** The extent of immune response to endotoxin (LPS) was assessed with intravital microscopy (IVM) of gut microvasculature. Video sequences were recorded and the extent of leukocyte activation was quantified.
- ❖ **Staining:** Brains of the animals were extracted post mortem and stained with tetrazolium chloride (TTC) to histologically confirm CNS injury and measure infarct size.

- ❖ Early CB2R activation **attenuates infarct size** after CNS injury
- ❖ Early CB2R activation **reduces the severity of the immune suppression** after CNS injury
- ❖ Late CB2R inhibition **reduces the immune suppression** after CNS injury
- ❖ CB2R-related modulation of leukocyte activation is involved in the impaired immune response following CNS injury

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