

ASSESSMENT OF IMMUNE SYSTEM ACTIVATION STATUS DURING THE COURSE OF HUNTINGTON'S DISEASE IN HD MOUSE MODELS

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BACKGROUND

A number of neurodegenerative diseases, characterised by progressive and selective death of neurons in the CNS, are accompanied by activation of the peripheral immune system. In Huntington's disease (HD), clinical and animal studies show elevated immune factors that are hallmarks of immune activity and the use of immunosuppressive regimens have shown beneficial effects in HD mice.. These results suggest a contributory role of the immune system in HD pathology, with immune based interventions offering potential therapeutic strategy to disease.

AIM

To assess peripheral and central nervous system (CNS) immune system activity in HD mouse models during disease course to determine if / when peripheral immunomodulation will be relevant for HD treatment.

METHOD

R6/2 mice were investigated pre and post-symptomatic stages for immune activity in the brain and periphery through the assessment of gene expression and protein levels of interleukin (IL)-1 β , IL-6, IL-10, IL-17 and tumor necrosis factor (TNF) α cytokines. Gene and cell surface (flow cytometry) expression of monocyte and macrophage activation (CD40 and OX40) and T cell activation (OX40 and CD25) markers were also measured.

RESULTS

At 14 weeks old (late-stage disease) cytokines and cell surface markers are elevated in several peripheral compartments as well as the brain. At 8 weeks (pre-symptomatic stage) however, immune activity is detectable in the periphery but not in the brain.

CONCLUSION

Immune activity in the periphery precedes immune activation in the CNS suggesting the peripheral immune system may promote activation of the CNS immune system during HD, possibly through the secretion of pro-inflammatory factors that can cross the blood brain barrier. Additionally, myeloid immune cells in the CNS and periphery display differing activated phenotypes during late stage HD with microglial cells presenting a predominantly M1 phenotype while monocyte/macrophages show a M2 predominating phenotype.

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