Pathogenesis of autoimmune neurodegeneration: What causes the immune system to destroy healthy neurons?

https://neurodegenerationresearch.eu/survey/pathogenesis-of-autoimmune-neurodegeneration-what-causes-the-immune-system-to-destroy-healthy-neurons/

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Research Abstract

The goal of this research is to determine under which conditions an autoimmune attack on neurons can occur. There is a growing interest in neuroimmunology, and data suggests that disorders such as Parkinson's disease and schizophrenia have an autoimmune component. The ideal disease for studying this phenomenon is, however, the sleep disorder narcolepsy with cataplexy (NC), where the hypocretin (hcrt) producing neurons in hypothalamus are lost. Genetic and epidemiological evidence suggest that the specific hcrt cell loss is caused by an autoimmune attack, but the trigger of this is unknown. As post doctoral fellow at Stanford Center for Sleep Sciences Dr. Birgitte R. Kornum has been involved in the discovery of two genetic associations in NC. This has implicated the P2Y11 receptor and DNA methyltransferase 1 (DNMT1) in the pathogenesis of NC and warrants further studies of these two proteins and their

functions in the immune system and the brain. The overarching aim of the research proposed here is to study autoimmune destruction of neurons, and how P2Y11 and DNMT1 contribute to the pathological process. Autoimmune destruction of neurons is prevented by several mechanisms. Negative selection of autoreactive T cells occurs during T cell maturation in the thymus. This process is, however, far from perfect and T cells with reactivity towards neuronal targets are instead controlled by other less well-understood mechanisms. These include inhibition of T cell activity by regulatory T cells, suppression of MHC expression in mature neurons, and a higher resistance in neurons to apoptotic signals from T cells. The experiments proposed here studies P2Y11 and DNMT1 in these processes using in vitro and in vivo models. Studies of patient samples from the Danish Center for Sleep Medicine will translate basic findings to the clinical situation. Together these studies will answer important questions, not only about NC, but about autoimmunity towards neurons in general.

Further information available at:

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