Expression of vitamin D receptor and metabolizing enzymes in multiple sclerosis-affected brain tissue

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Research question and background

A low vitamin D status, as well as several vitamin D related genetic polymorphisms have been associated with an increased risk of developing MS. Additionally, a low vitamin D status has been associated with more relapses and a higher EDSS-score in MS patients. How vitamin D metabolism affects MS pathophysiology is not understood. Since vitamin D gains access to the central nervous system (CNS), we hypothesized vitamin D to interact with the disease process of MS within the CNS.

Methods and tissues used

We studied the expression of vitamin D receptor (VDR) and related enzymes, including $1,25(OH)_2$D-24-hydroxylase (24-OHase; CYP24A1) and 25(OH)D-1α-hydroxylase (CYP27B1), in CNS tissues of 39 MS patients and 20 controls and in primary human microglia and astrocytes *in vitro*.

Results and conclusion

In control and MS normal-appearing white matter (NAWM), nuclear VDR immunostaining was observed in oligodendrocyte-like cells, human leukocyte antigen (HLA)–positive microglia, and glial fibrillary acidic protein–positive astrocytes. There was a 2-fold increase in VDR transcripts in MS NAWM versus control white matter ($p = 0.03$). In chronic active MS lesions, HLA-positive microglia/macrophages showed nuclear VDR staining; astrocytes showed nuclear and cytoplasmic VDR staining. Staining for 24-OHase was restricted to astrocytes. VDR and CYP27B1 mRNA expressions were increased in active MS lesions versus NAWM ($p < 0.01$, $p = 0.04$, respectively). In primary human astrocytes in vitro, the active form of vitamin D, $1,25(OH)_2D_3$, induced upregulation of VDR and CYP24A1. Tumor necrosis factor and interferon-γ upregulated CYP27B1 mRNA in primary human microglia and astrocytes. Increased VDR expression in MS NAWM and inflammatory cytokine–induced amplified expression of VDR and CYP27B1 in chronic active MS lesions suggest increased sensitivity to vitamin D in NAWM and a possible endogenous role for vitamin D metabolism in the suppression of active MS lesions.