THE CSF LEVELS OF CCL-2 (MCP-1) ARE ASSOCIATED WITH A FASTER COGNITIVE DECLINE IN PRODROMAL ALZHEIMER’S DISEASE

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Chemokine (C-C motif) receptor 2 (CCR2) is expressed on microglia, and mediates the accumulation of mononuclear phagocytes at sites affected by inflammation. It has been suggested that CCR2 and its main ligand CCL-2 (MCP-1) are involved in the beta-amyloid (Aβ) metabolism during the early stages of Alzheimer’s disease (AD). We therefore measured the levels of CCL2 and two other CRC2 ligands, i.e. CCL-11 (eotaxin) and CCL-13 (MCP-4), in the CSF and plasma of 30 controls and 119 patients with mild cognitive impairment (MCI) at baseline. During clinical follow-up 52 (44%) of the MCI patients were clinical stable for 5.2 years, 47 (39%) developed AD and 20 (17%) developed other dementias. The baseline levels of CCL-2, CCL-11 and CCL-13 were not significantly changed in the CSF or plasma of MCI patients who subsequently developed AD when compared to controls. However, in patients with prodromal AD, the CCL-2 levels in CSF correlated with an increased rate of cognitive decline (R=0.42, p=0.004). Moreover, prodromal AD cases in the highest tertile of CSF CCL-2 exhibited increased cognitive decline as well as a shorter time to development of dementia compared to those in the lowest tertile. In conclusion, CCL-2 seems to be associated with an increased cognitive deterioration rate in cases affected with prodromal AD. CCL-2 might be a therapeutic target for new therapies aiming at slowing down the disease progression rate of AD. Moreover, CCL-2 in CSF might be used as a surrogate marker in clinical trials using anti-inflammatory agents for prodromal AD.