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COGNITIVE IMPAIRMENT IN RHEUMATOID ARTHRITIS IS ASSOCIATED WITH CHANGES IN PERIPHERAL LYMPHOCYTE SUBSETS, CYTOKINES AND NEUROTROPHIC FACTORS

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Rheumatoid Arthritis (RA) is presented with extra-articular manifestations including cognitive impairment. The underlying mechanisms of these cognitive changes remain unclear. The present study investigated the relationship between inflammatory biomarkers, neurotrophines, autoantibodies against myelin sheath and cognitive performance in RA patients with active and controlled disease. To this end, PBMCs and plasma samples were obtained of 35 controlled RA, 67 active RA and 30 healthy controls. The PBMCs were immunophenotyped by flow cytometry to investigate subpopulations of B and T lymphocytes. Levels of cytokines were measured by means of cytometric bead array and, neurotrophines, anti-MOG, anti-MBP and S-100b were measured by ELISA. Memory, attention, executive function, depression and stress were evaluated by means of structured interview all participants of this study. RA patients, especially active RA, had worse performance in all cognitive testes when compared with control group (all $p < 0.05$). RA patients had higher levels of NKT, NK, Th17, immature B cells (CD19+CD24+CD38+), plasma cells, TNF- α , IL-10, IL-4, IL-6, IL-2, BDNF, and lower levels of Tc, Treg cells and GDNF than control group (all $p < 0.05$). Active RA group had significantly higher levels of anti-MBP IgG, anti-MOG IgG and S100 β protein than controls (all $p < 0.0001$). Positive associations were found between executive function and NKT, CD19+CD24+CD38+, IL-2, IL-4, IL-6 and TNF- α (all $p < 0.05$). Negative correlation were found between attention and Tc, Treg, CD4/CD8 and IL-6, and between memory and CD19+CD24+CD38+, IL-4, IL-6 and BDNF (all $p < 0.05$). In conclusion, RA patients were cognitively impaired in all cognitive domains tested in this study. This impairment was major in active disease than controlled disease and control group. Furthermore, our results showed that RA is followed by remodeling of peripheral immune system and higher production of autoantibodies against proteins of central nervous system. These alterations of peripheral environment are potentially involved in the cognitive impairment of RA.