Journal of Neuroimmunology 251 (2012) 73–79

Contents lists available at SciVerse ScienceDirect

Journal of Neuroimmunology

journal homepage: www.elsevier.com/locate/jneuroim

Disease-specific expression of the serotonin-receptor 5-HT_{2C} in natural killer cells in Alzheimer's dementia

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ARTICLE INFO

Article history:
Received 9 February 2012
Received in revised form 14 April 2012
Accepted 3 June 2012

Keywords:
Aging
Alzheimer's disease
β-amyloid peptide
Dopamine-receptor
Leukocyte
Natural killer (NK) cell
Peripheral blood mono-nuclear cell (PBMC)
Serotonin-receptor

ABSTRACT

Alzheimer's dementia (AD) is a degenerative brain disorder characterized mainly by cholinergic failure, but other neuro-transmitters are also deficient especially at late stages of the disease. Misfolded β-amyloid peptide has been identified as a causative agent, however inflammatory changes also play a pivotal role. Even though the most prominent pathology is seen in the cognitive functions, specific abnormalities of the central nervous system (CNS) are also reflected in the periphery, particularly in the immune responses of the body. The aim of this study was to characterize the dopaminergic and serotonergic systems in AD, which are also markedly disrupted along with the hallmark acetyl-choline dysfunction. Peripheral blood mono-nuclear cells (PBMCs) from demented patients were judged against comparison groups including individuals with late-onset depression (LOD), as well as non-demented and non-depressed subjects. Cellular sub-populations were evaluated by mono-clonal antibodies against various cell surface receptors: CD4/CD8 (T-lymphocytes), CD19 (B-lymphocytes), CD14 (monocytes), and CD56 (natural-killer (NK)-cells). The expressions of dopamine D_3 and D_4, as well as serotonin 5-HT_{1A}, 5-HT_{2A}, 5-HT_{2B} and 5-HT_{2C} were also assessed. There were no significant differences among the study groups with respect to the frequency of the cellular sub-types, however a unique profound increase in 5-HT_{2C} receptor exclusively in NK-cells was observed in AD. The disease-specific expression of 5-HT_{2C}, as well as the NK-cell cyto-toxicity, has been linked with cognitive derangement in dementia. These changes not only corroborate the existence of bi-directional communication between the immune system and the CNS, but also elucidate the role of inflammatory activity in AD pathology, and may serve as potential biomarkers for less invasive and early diagnostic purposes as well.

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doi:10.1016/j.jneuroim.2012.06.003