PROTEOMIC ANALYSIS OF CEREBROSPINAL FLUID IN MILD COGNITIVE IMPAIRMENT

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Mild cognitive impairment (MCI) is a common syndrome in elderly people that can progress to Alzheimer's disease (AD) and other primary causes of vascular dementia (VaD), Lewy body disease (LBD), and frontotemporal dementias (FTD) or to be a part of normal brain aging. The annual rate of progression from MCI to AD is about 12-15%. Magnetic resonance imaging (MRI), positron emission tomography (PET) and cerebrospinal fluid (CSF) biomarkers are considered to be the most promising for early detection and accurate differentiation of AD from other primary causes of dementia. Within the scope of the project "*Detection and tracking of biological markers for early therapeutic intervention in sporadic Alzheimer's disease*", in which biochemical, imaging, and genetic biomarkers are correlated in order to detect AD in early stages, the concentrations of total τ protein (t-τ) and amyloid β_{1-42} ($A\beta_{1-42}$) were analyzed using ELISA kits in CSF of 126 patients of which 54 were patients with probable AD, 30 with MCI, 9 with VaD, 4 with LBD, 11 with FTD. We also analyzed 18 healthy controls. Cut-off levels for $A\beta_{1-42}$ and t-τ were derived from ROC curve analysis, when the sum of specificity and sensitivity was maximized. The results showed that 23.3% of MCI subjects had $A\beta_{1-42}$ and t-τ levels as patients with probable AD, while 53.3% of them had either $A\beta_{1-42}$ lower or t-τ higher than cut-off levels. As a follow-up period of at least 5 years is needed to assess reliably MCI patients who will develop AD, only then will we be able to conclude if defined cut-off levels indeed distinguish MCI patients that will progress to AD from those who will not. Additionally, phosphorylated τ (p-τ231) measured in 36 subjects was shown to distinguishing AD from healthy controls with sensitivity of 76.5% and specificity of 80%. We hope that by increasing the number of subjects analyzed, higher sensitivity and specificity of $p\text{-}\tau_{231}$ and other forms of p-τ ($p\text{-}\tau_{199}$ and $p\text{-}\tau_{181}$) will be obtained. In conclusion, determination of p-tau biomarkers in CSF and extended follow-up along with regular imaging of brain structure and activity in MCI patients should improve diagnostic accuracy of CSF biomarkers in detection of early AD. *Supported by the Croatian Science Foundation grant. no. 09/16*.

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