OXIDIZED PROTEINS IN THE CEREBROSPINAL FLUID AS PUTATIVE BIOMARKERS FOR ALZHEIMER’S DISEASE

M.K. Herbert, M.M. Verbeek, H.B. Kuiperij

Department of Neurology and Donders Institute for Brain, Cognition and Behaviour, Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands

Introduction: Oxidative stress is a general, early feature in neurodegenerative diseases, including Alzheimer's disease (AD). But importantly, it has been shown that oxidative stress leads to the oxidation of specific proteins, which include for AD the peptidyl-prolyl isomerase Pin1, glutamine synthetase (GS) and amyloid β (Aβ). These proteins, in their oxidized form, may serve as new biomarkers for an early diagnosis of AD.

Aims: To develop sensitive assays for the quantification of oxidized GS, Pin1 and Aβ in cerebrospinal fluid (CSF), and to clinically validate their use as diagnostic biomarkers for AD.

Methods: The amount of protein carbonyls and/or methionine oxidation is used as an index for protein oxidation. Sensitive ELISAs will be developed for the quantification of GS, Pin1 and Aβ. Subsequently, these assays are combined with the ELISAs for protein carbonyls/methionine oxidation in order to specifically measure oxidized GS, Pin1 and Aβ.

Results: We successfully produced and isolated recombinant GS and Pin1 protein and developed protocols for the oxidation of these proteins and Aβ peptides. Furthermore, we have developed ELISAs for the oxidized form of Pin1, GS and Aβ. We will present the results of the analysis of these oxidized proteins in CSF of AD patients compared to controls.

Conclusions: We have developed novel ELISAs in which the proteins GS, Pin1 and Aβ, respectively, are detected specifically in their oxidized form. These ELISAs are used in clinical cohorts to evaluate the potential of these oxidized proteins in CSF as early, diagnostic biomarkers for AD.