A COMBINED ACID PRE-TREATMENT AND NEUTRALIZATION PROTOCOL IMPROVES CSF GLUTAMINE SYNTHETASE DETECTION BY ELISA

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

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

Introduction: Glutamine synthetase (GS) is an enzyme that catalyses the conversion of potentially neurotoxic glutamate and ammonia to glutamine in astrocytes. Since loss of GS enzyme activity in the brain is linked to Alzheimer's disease (AD), it was proposed previously that GS may be a potential cerebrospinal fluid (CSF) biomarker for the diagnosis of AD. Indeed, GS can be detected in CSF of AD patients at higher levels than those seen in control patients.

Aims: To develop a sensitive ELISA to measure GS in CSF and to evaluate the use of CSF GS as a biomarker for AD.

Methods: We developed an ELISA to quantify GS protein in CSF and developed a CSF acid pre-treatment and neutralization protocol to improve the quantification of GS in CSF by ELISA.

Results: We showed that the use of a combined acid pre-treatment and neutralization protocol for CSF substantially improves the detection of GS in CSF. Furthermore, this CSF pre-treatment protocol does not only enhance the detection of GS, but also of several other CSF proteins, including amyloid beta and myelin basic protein.

Conclusions: The use of an acid pre-treatment and neutralization protocol for CSF improves the quantification of GS and other CSF proteins. This enhancement may be due to a combined effect of disassembly of CSF protein complexes upon acidification and optimization of the pH of CSF upon neutralization for measurement of the proteins by ELISA. Application of this technique may improve several CSF biomarker assays for AD and other neurodegenerative diseases.